vol 17 no 8 AUGUST 60

American Journal of Hospital Pharmacy

official publication of the American Society of Hospital Pharmacists

FORMERLY The BULLETIN

MUTUAL AREAS OF COOPERATION BETWEEN PHARMACY AND NURSING

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American Journal of Hospital Pharmacy

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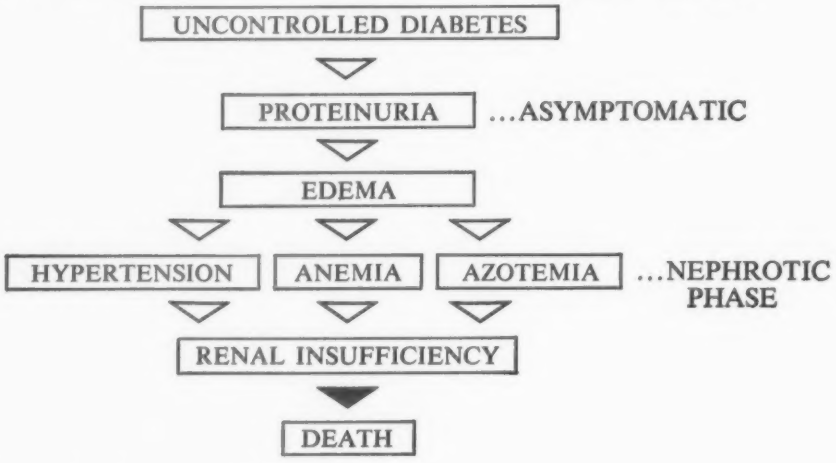
Source: Whitehouse, F. W.: Postgrad. Med. *24*:54, 1958.

NATURAL HISTORY OF DIABETIC NEPHROPATHY



Adapted from Whitehouse, F. W.: *op. cit.*

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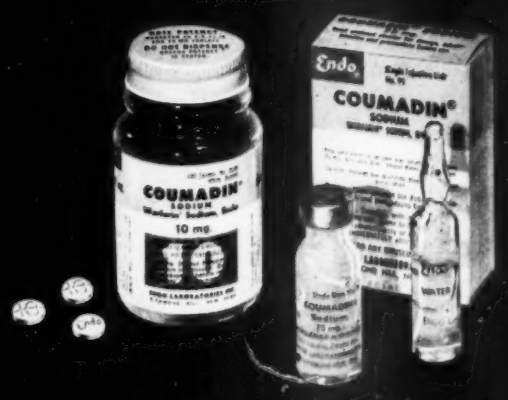

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Average Dose: Initial, 40-60 mg. For elderly and/or debilitated patients, 20-30 mg.

Maintenance, 5-10 mg. daily, as indicated by prothrombin time determinations.

1. Baer, S., et al.: J.A.M.A. 167:704, June 7, 1958.
2. Moser, K. M.: Disease-a-Month, Chicago, Yr. Bk. Pub., Mar., 1960, p. 13.

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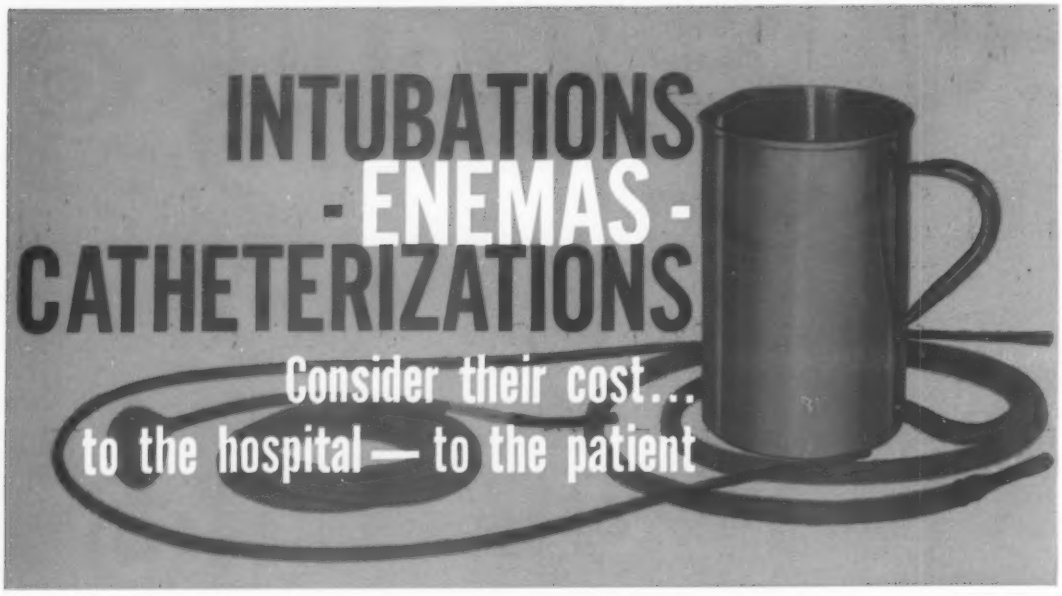

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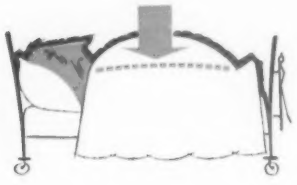

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1. Kareha, L.G. et al, W.Jour.S.O.&G., 66:220, 1958
2. Stone, M.L. et al, Amer.J.Surgery, 97:191, 1959

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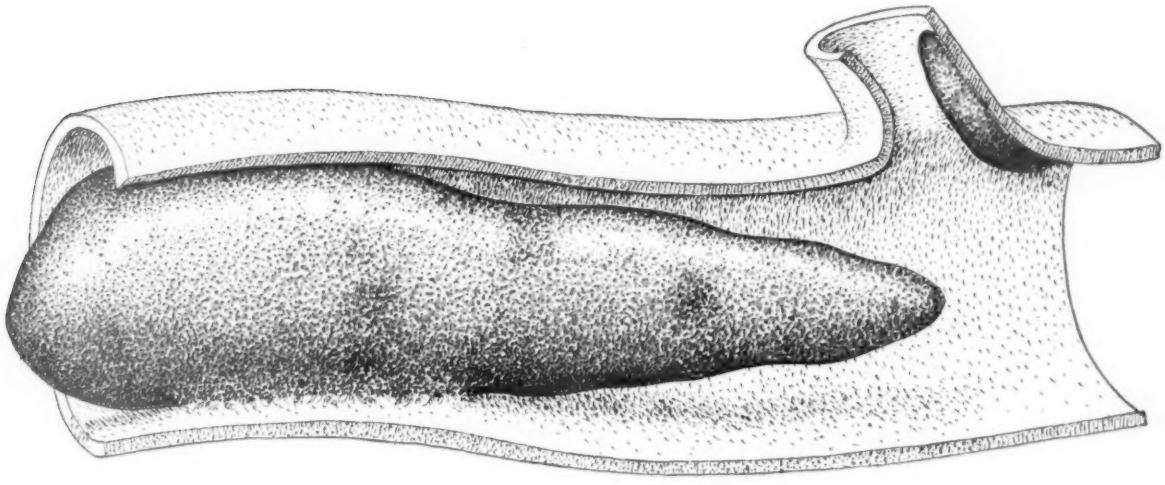

THROMBOLYSIN, supplemented by anticoagulant therapy, can greatly reduce mortality and morbidity in thrombophlebitis, phlebothrombosis, pulmonary embolism, and certain arterial thrombi.* Recently formed clots are lysed rapidly, usually in 24 hours.

to lyse thrombi

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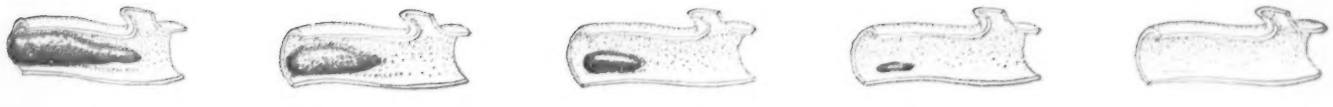

THROMBOLYSIN®

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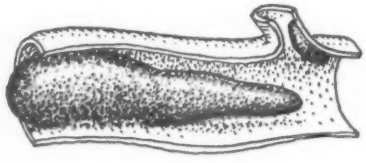
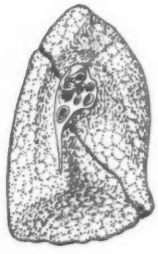
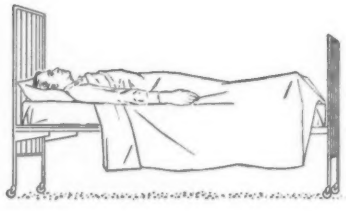
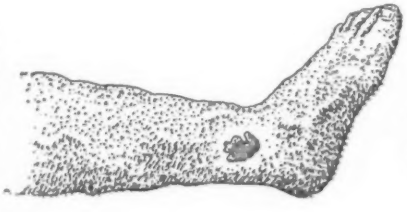
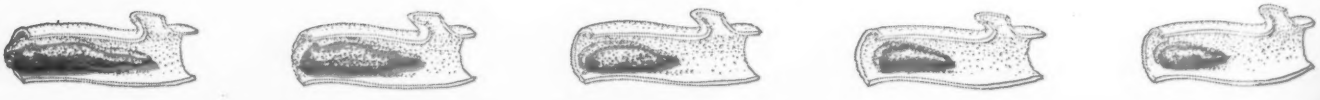
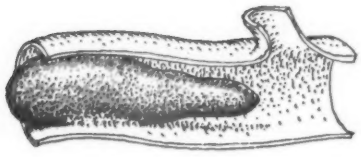
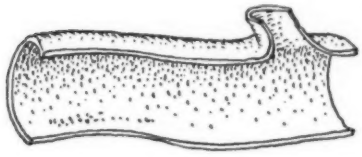
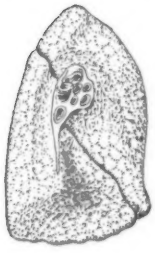
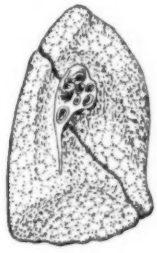
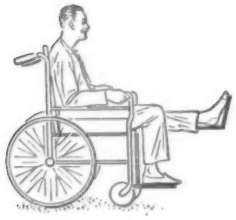
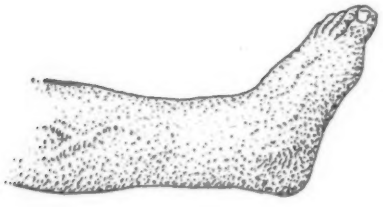
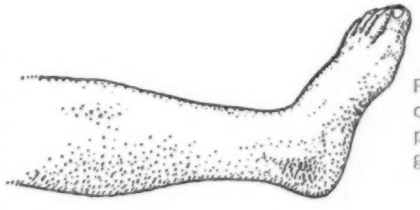
early use greatly reduces morbidity and mortality in thrombophlebitis, phlebothrombosis, pulmonary embolism, and certain arterial thrombi

Results of therapy	Bed rest
Effect on intravascular thrombi	 Clot may form permanent obstruction to blood flow. New clots may form.
Effect on pulmonary emboli	 Sudden death from pulmonary embolism is an ever-present hazard. One or more nonfatal pulmonary emboli may result in irreversible lung damage or secondary pneumonia.
Effect on duration of illness and convalescence	 Weeks of hospitalization or bed rest at home are commonly required in the management of thrombophlebitis, phlebothrombosis, pulmonary embolism, and arterial thrombosis.
Frequency and severity of postphlebitic syndrome	 Chronic leg swelling, severe secondary varicose veins, and leg ulcers are common sequelae.



Anticoagulant + Bed rest		THROMBOLYSIN + Anticoagulant + Bed rest	
	Anticoagulants cannot remove formed clot. However, they help prevent its extension and minimize formation of new clots.		Recently formed intravascular clots are lysed and the formation of new clots is inhibited. Circulation is restored and maintained, with rapid symptomatic relief.
	The careful use of anticoagulants reduces the occurrence of pulmonary emboli.		The incidence and severity of pulmonary emboli are greatly reduced since THROMBOLYSIN acts to remove thrombi before they can become emboli.
	Thromboembolic illness and convalescence are shortened.		A striking reduction is observed in the duration of hospital stay, bed rest, and convalescence.
	The incidence and severity of the postphlebitic syndrome are reduced.		Postphlebitic complications are prevented or greatly minimized.

What is THROMBOLYSIN?

THROMBOLYSIN is Fibrinolysin, Human. It is prepared by activating the profibrinolysin-rich Fraction III – 3 of pooled human plasma with highly-purified streptokinase and then lyophilizing it. THROMBOLYSIN helps restore the natural equilibrium between clot formation and clot lysis, thereby enhancing the ability of the blood to maintain normal flow.

In What Conditions is it Indicated?

THROMBOLYSIN is indicated in thrombophlebitis, phlebothrombosis, pulmonary embolism, and certain arterial thrombi.

*(NOTE: *Successful lysis of thrombi of major cerebral vessels has been reported. However, additional experience is required to define the indications and contraindications of therapy in such patients. THROMBOLYSIN has also been administered to patients with acute myocardial infarction, but the scope of this work is still too limited to permit conclusions about its safety or benefit.*)

When Should Therapy be Initiated?

Treatment with THROMBOLYSIN should be started as soon as possible after a thrombus has formed. Blood clots begin to organize shortly after formation and may become encased in a layer of endothelial cells, making them resistant to the action of THROMBOLYSIN. Usually, more rapid lysis can be expected to take place when treatment is initiated within five days after a thrombus has formed; however, in some cases successful lysis has been accomplished when treatment was not initiated for several weeks after thrombus formation.

Can THROMBOLYSIN be Given to Patients Being Treated with Anticoagulants?

Yes. Patients who have been on anticoagulant therapy can be expected to improve when THROMBOLYSIN is added to their program of treatment.

Does THROMBOLYSIN Increase the Incidence of Embolism?

Clinical studies indicate that it does not. In fact, if any evidence of embolization should appear, it is important to continue THROMBOLYSIN until symptoms have disappeared.

What is the Dosage?

The dosage most frequently used by investigators has been 4 vials (200,000 MSD units) per day by intravenous infusion. This is usually administered by giving 1 vial per hour for 4 consecutive hours. Alternatively, 1 vial (50,000 MSD units) per hour may be given for 2 consecutive hours and repeated in 3 to 6 hours. The dosage range is 1 vial (50,000 MSD units) to 2 vials (100,000 MSD units) an hour, by intra-

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treated rapidly
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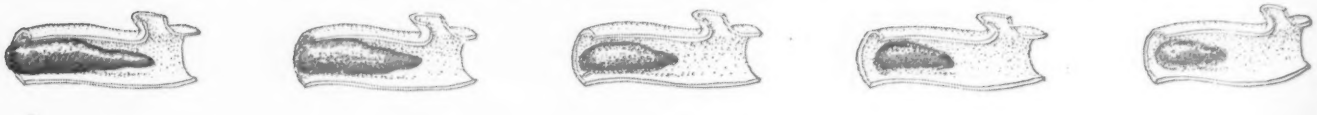

venous drip, for 1 to 6 hours, depending on the nature of the clot and the response of the patient. Most patients respond in one day; those who do not may require additional doses for three or four successive days.

Patients not under active treatment with anticoagulants at the time of the thromboembolic episode:

New clot formation is unlikely to occur during the administration of THROMBOLYSIN, so that anticoagulants may be unnecessary in this period. However, the fibrinolytic activity of THROMBOLYSIN persists only 3 to 4 hours after cessation of infusion; in patients subject to thrombosis, provision should be made to provide adequate therapeutic anticoagulant effect at this time.

Patients under active treatment with anticoagulants:

Within recommended dosages, THROMBOLYSIN produces only minor alterations in the clotting mechanism: the prothrombin time is generally increased by only a few seconds, the Lee-White clotting time by only 1 to 4 minutes, and the fibrinogen levels generally decrease by about 30 percent of control values. In themselves, these alterations are probably of no clinical significance. In patients on concurrent anticoagulant therapy in whom the clotting mechanism is depressed to midtherapeutic levels, the small additional depression due to THROMBOLYSIN should produce no added danger; however, the addition of THROMBOLYSIN may be hazardous when the therapeutic anticoagulant level already threatens to exceed safe limits.

What Other Precautions are Necessary?

THROMBOLYSIN is contraindicated in the presence of a hemorrhagic diathesis or hypofibrinogenemia. Fibrinolytic activity usually increases spontaneously for a short period after anesthesia or surgery. Therefore, THROMBOLYSIN should be used with caution because lysis of the clots at the operative site may occur.

Bleeding from open wounds or recent operative sites can occur during therapy. Usually this has been observed only in patients receiving both an anticoagulant and THROMBOLYSIN. In such cases, the bleeding was controlled by the use of plasma or whole blood transfusions. A specific antagonist to the anticoagulant may also be used.

What Side Effects May Occur?

Febrile reactions may occur, but these are rarely severe. When they do occur, the temperature usually rises rapidly to a peak, then returns to normal within 24 hours. In some patients, a rise in temperature above 1.5 to 2 degrees F. is accompanied by chills, nausea, vomiting, dizziness, headache, muscle pain, back pain, tachycardia, or hypotension.

How is it Supplied? 100-cc. vials containing 50,000 MSD units.

to lyse thrombi

OMBOLYSIN®

FIBRINOLYSIN, HUMAN

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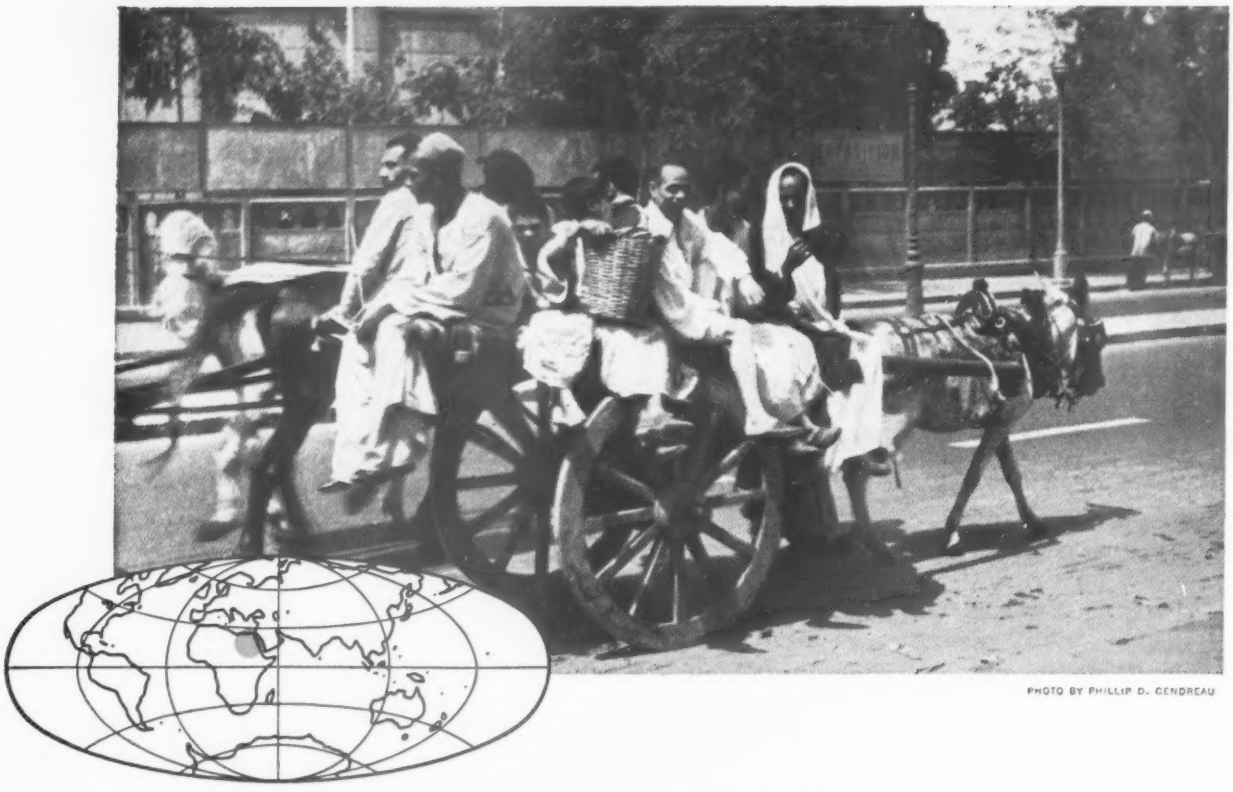

PHOTO BY PHILLIP D. CENDREAU

world-wide evidence favors Furoxone for bacterial diarrheas

In Egypt, Furoxone® effective against shigella strains now resistant to other antimicrobials

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FUROXONE was tested in light of evidence that shigella strains resistant to sulfonamides, tetracyclines and chloramphenicol now exist. Observations: "All shigella isolated were sensitive in vitro to [FUROXONE]". Clinically, FUROXONE "significantly reduces the duration and severity of the diarrhea and effects bacteriological cure . . . . The absence of toxic or side effects gives [FUROXONE] an advantage not possessed by the other drugs in current use."

Musgrave, M. E., and Arm, H. G.: Antibiotic Med. & Clin. Therapy 7:17 (Jan.) 1960.

FUROXONE LIQUID: a pleasant orange-mint flavored suspension containing FUROXONE 50 mg. per 15 cc., with kaolin and pectin ■ for patients of all ages (may be mixed with infant formulas, passes through a standard nursing nipple) ■ Supply: bottles of 240 cc. **FUROXONE TABLETS:** 100 mg., scored, bottles of 20 and 100.

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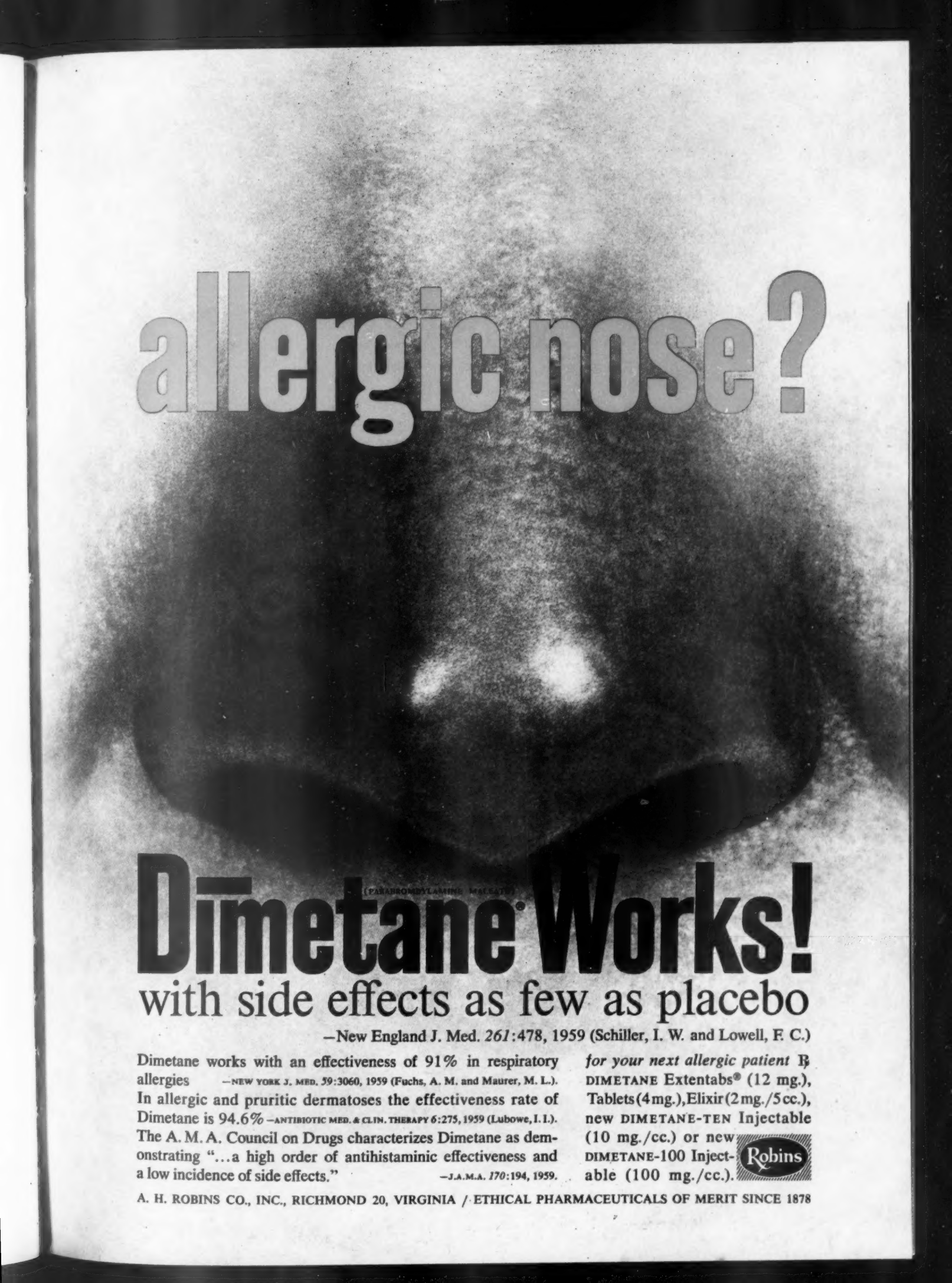

with side effects as few as placebo

—New England J. Med. *261*:478, 1959 (Schiller, I. W. and Lowell, F. C.)

Dimetane works with an effectiveness of 91% in respiratory allergies —NEW YORK J. MED. *59*:3060, 1959 (Fuchs, A. M. and Maurer, M. L.).

In allergic and pruritic dermatoses the effectiveness rate of Dimetane is 94.6% —ANTIBIOTIC MED. & CLIN. THERAPY *6*:275, 1959 (Lubowe, I. I.).

The A. M. A. Council on Drugs characterizes Dimetane as demonstrating "...a high order of antihistaminic effectiveness and a low incidence of side effects." —J.A.M.A. *170*:194, 1959.

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References: (1) Ayd, F. J., Jr.: New England J. Med. *261*:172, 1959. (2) Morgan, D. R., and van Leent, J. P.: M. J. Australia *45*:696, 1958.

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References: 1. Sadove, M. S.: A preliminary report on Carbocaine, a new local anesthetic. Submitted for publication. 2. Luduena, F. P.; Hoppe, J. O.; Coulston, F., and Drobeck, H. P.: The pharmacology and toxicology of mepivacaine, a new local anesthetic, *Toxicol. & Appl. Pharmacol.* To be published. 3. Rovenstine, E. A.: Personal communication. 4. Young, J. A.: Upper arm block with Carbocaine (mepivacaine), a new anesthetic agent, *Anesth. & Analg.* To be published. 5. Griesser, Gerd: Erfahrungen mit einem neuen Lokalanestheticum, *Anaesthesist* 6:364, Oct., 1957.

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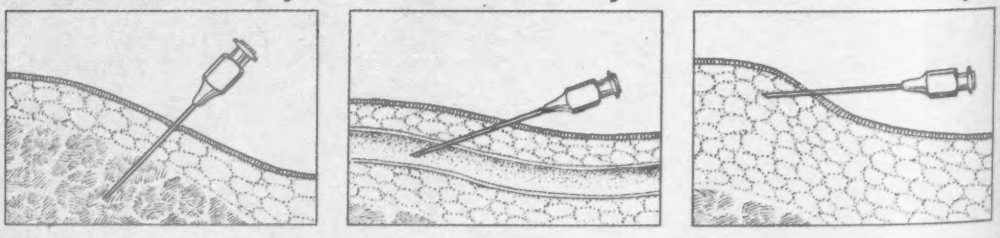

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*Council on Drugs: New and Nonofficial Drugs, Philadelphia, J. B. Lippincott Co., 1960, p. 732

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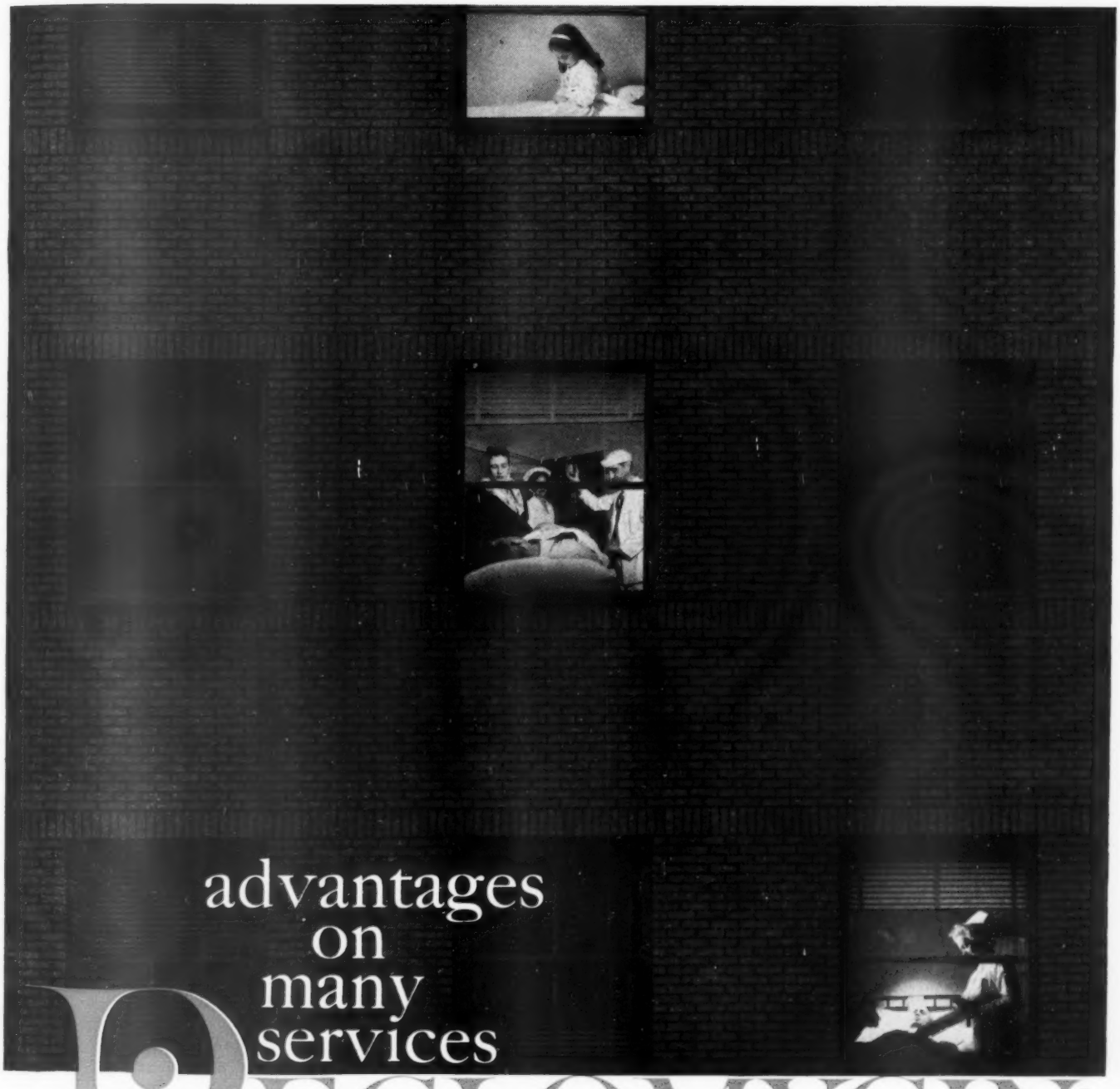

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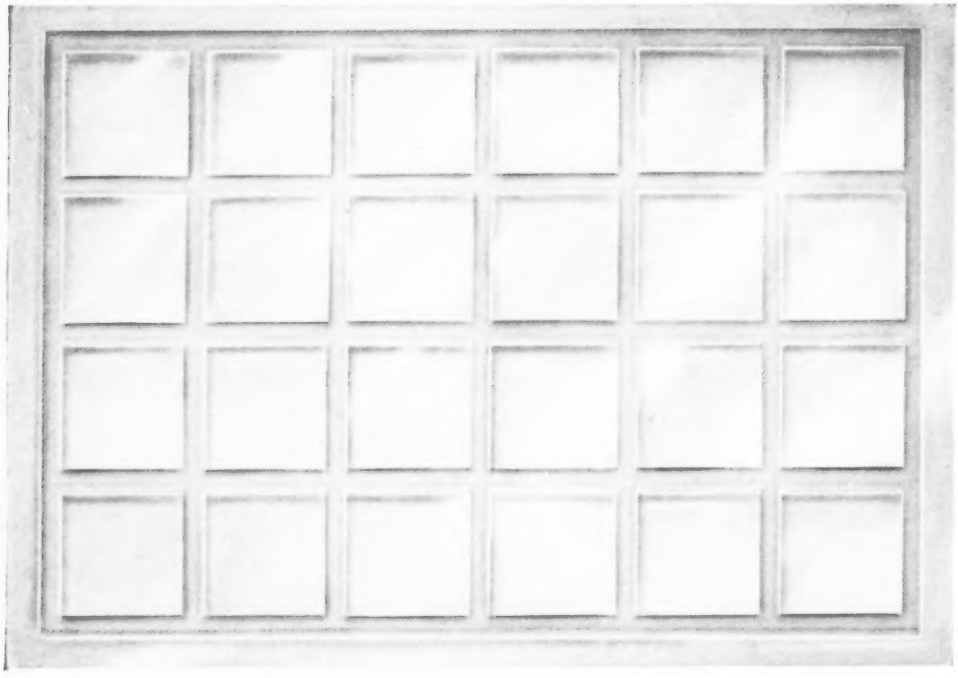

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DEAR MEMBERS:

During the past year the Society has mourned the loss of two honorary members who were great leaders in the development and progress of Hospital Pharmacy.

Dean Edward Spease and Mr. H.A.K. Whitney symbolize the advancement in our field because they fostered better standards of practice through education and training.

The Executive Committee has agreed that the establishment of the Whitney-Spease Scholarship Fund of the ASHP will be an appropriate memorial by providing assistance to chosen graduate students in Hospital Pharmacy.

This is an invitation to you to participate in perpetuation of the contributions of Edward Spease and Harvey Whitney by supporting graduate education through the Whitney-Spease Scholarship Fund of the ASHP.

Your contribution will be beneficial to you and to Hospital Pharmacy. Please use the attached form to send your contribution.

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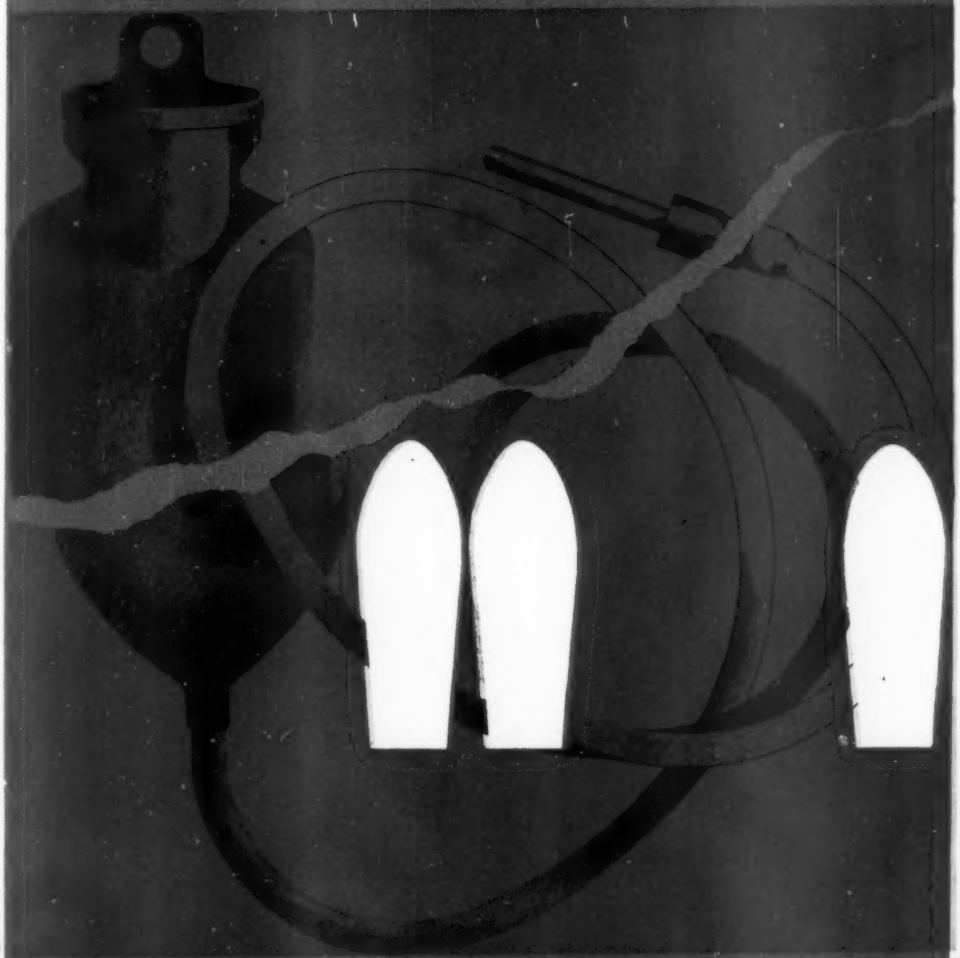

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Midwest Association of Sister Pharmacists

Activities of the Midwest Association of Sister Pharmacists are covered in the group's regular publication known as "The Adjuvant." According to a recent issue, a number of their members attended the Pharmacy Section of the Tri-State Hospital Assembly and a summary of papers presented is included in the publication.

Also in conjunction with the Tri-State Assembly, the members of the Midwest Association of Sister Pharmacists met at the Palmer House following the Pharmacy Section meetings. Also invited were members of the Executive Committee of the Illinois Society of Hospital Pharmacists. The topics for discussion were (a) to evaluate the advantages and to determine the means for greater cooperation between the M.A.S.P. and the I.S.H.P.; and (b) to evaluate the possibility of institutional membership of the M.A.S.P. in the Illinois Hospital Association.

Southern Appalachian Society

Members of the Southern Appalachian Society of Hospital Pharmacists held their June meeting in the Terrace Room of the Beckley Hotel in Beckley, West Virginia. Following a luncheon, sponsored by E. R. Squibb and Sons Pharmaceutical Company, the business meeting was called to order.

Matters considered during the business session included the possibility of recommending a pharmacist to the State Board of Pharmacy, consideration of legislation affecting hospital pharmacy, appointment of a delegate to the Annual Meeting in Washington, D. C., and the status of the Society's finances.

In a round table discussion during the program, subjects covered included the Schwartz system *versus* open shelving, inventory control, hospital pharmacy laws in Ohio, West Virginia, and Kentucky, and drug rooms in hospitals.

Northern California Society

The 139th meeting of the Northern California Society of Hospital Pharmacists was held at St. Luke's Hospital in San Francisco on Tuesday, June 14. This was a joint meeting with the local chapter of the American Pharmaceutical Association. Mr. Stephen Dean served as program chairman for the meeting.

The principal speaker was the Reverend James T. Golder, authority on the cause and effects of alcoholism and a former member of the Governor's Advisory Board on Alcoholism in the State of Washington. In his discussion, he described the "problem drinker," and listed the progressive steps taken from this stage to the early stages of alcoholism and finally culminating in the later stages and complete surrender of the individual to the disease. He then spoke of the problems of curing the alcoholic, referring to the effectiveness of the Alcoholics Anonymous organization.

Announcements were made and particular reference was made to the fact that Mr. Claude Busick has recently been appointed a member of the Board of Directors of the Pharmaceutical Institute, the first hospital pharmacist ever to hold this post.

Southern California Society

The regular monthly meeting of the Southern California Society of Hospital Pharmacists was held June 8, 1960, at the Upjohn Pharmaceutical Company building in Los Angeles. The meeting was called to order at 8 P.M. by President Wendell Hill.

During the business session, reports were heard from Mr. Joe Winestock, Chairman of the Education and Legislation Committee, and Mr. Chester Bazil, Chairman of the Scholarship Committee. The Southern California Society voted to offer one or more scholarships of one hundred dollars each, plans to be worked out with the University of Southern California School of Pharmacy.

Mr. Joe Beckerman reported on a recent meeting of the Southern California Pharmaceutical Association which featured a discussion of the proposed Code of Ethics.

Two representatives were named to attend the Annual ASHP Convention in Washington. They are Wendell Hill and Frank Gianetti.

Connecticut Society

The regular meeting of the Connecticut Society of Hospital Pharmacists was held at the Hotel Statler in Hartford on June 29. The meeting was preceded by a buffet supper sponsored by Organon, Inc.

The results of the recent election were announced. New officers for the 1960-61 term are: *President,* Louis C. Annino, Middlesex Memorial Hospital, Middletown; *Vice-President,* David Burack, Mt. Sinai Hospital, Hartford; *Secretary,* William S. Brown, Grace-New Haven Community Hospital, New Haven; and *Treasurer,* Sister Maria Lucia, Hospital of St. Raphael, New Haven.

Georgia Society

The Georgia Society of Hospital Pharmacists held a meeting in conjunction with the Southeastern Hospital Conference in Miami Beach on May 4. At this time the new officers for the coming year were installed including *President,* Herbert Dittmer, V. A. Hospital, Augusta; *Vice-President,* Lt. Thomas DeCillis, U. S. Public Health, Savannah, and *Secretary-Treasurer,* Sister Mary Maurice, St. Joseph's Hospital, Augusta.

Idaho Society

The seventh meeting of the Idaho Society of Hospital Pharmacists was held at Magic Valley Memorial Hospital, Twin Falls, on Saturday, June 4, 1960. The meeting was called to order by President Herbert Whitby at 10 A.M.

The President read several letters of communication in regard to affiliation with the ASHP. He noted the requirement to affiliate with the ASHP must be ten or more members. Louis P. Jeffrey, National Chairman of the Committee on Membership and Organization, and Vernon O. Trygstad, National President of the ASHP, made application to I.S.H.P. to bring the organization up to the required number. Their applications were accepted. During discussion of affiliation, a motion was made by Truman Barlow and seconded by

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Donald Ness that application be submitted for affiliation with the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS. The motion passed unanimously and the necessary application has been made to the national organization.

Donald Ness mentioned that the Idaho State Pharmaceutical Association established ideas with a view to include regulations to cover hospital pharmacies. Herbert Whitby was asked to write to the president of I.S.P.A. and Donald Ness is planning to meet with the Board of Directors at their June meeting.

Following the business meeting, election was held. The following officers were re-elected: *President,* Herbert Whitby; *Vice-President,* Donald Ness; and *Secretary-Treasurer,* Sister M. Verita.

The program consisted of an interesting and educational talk on insulin preparations and uses given by Mr. Don Johnson, representative of Eli Lilly Company. A luncheon sponsored by Wyeth Laboratories was arranged by Dale Wilson.

The next meeting will be at Boise, Idaho, October 17, 1960 in conjunction with the Idaho Hospital Association Convention.

Illinois Society

The Executive Committee of the Illinois Society of Hospital Pharmacists met on May 24 at the Illinois Research and Education Hospital in Chicago. The meeting was called to order by President William Collins. Communications were read and plans were discussed for joint meetings and cooperation with the Midwest Association of Sister Pharmacists which is also in Illinois. According to the decisions made, the Midwest Association will maintain its identity but the two groups will attempt to work more closely.

There was some discussion regarding changes in the Constitution and By-Laws and succession of elected officers to the presidency.

General programing for the coming years was discussed with specific plans for places and time of meetings.

Mr. Nelson Kitsuse gave a report of the special committee forming policies between the Illinois Society of Hospital Pharmacists and the Illinois Hospital Association. Mr. Edgar Duncan made a motion that this committee have the power to set dates for the open meetings that would be held at the headquarters of the American Hospital Association in Chicago. The motion carried.

Louisiana Society

Miss Gladys Hebert, Pharmacist at Charity Hospital, New Orleans, is the new President of the Louisiana Society of Hospital Pharmacists. Other officers recently elected are William M. Hanna, U. S. Public Health Service Hospital, New Orleans, *Vice-President;* Anna Mae L. Cisneros, Ochsner Foundation Hospital, New Orleans, *Secretary;* and Herbert J. Mang, also of Ochsner Foundation Hospital, New Orleans, *Treasurer.*

The installation was held May 26 at Arnaud's Restaurant. It was followed by a dinner sponsored by I. L. Lyons and Company, Drug Wholesaler. Mr. William P. O'Brien, Inspector for the Louisiana Board of Pharmacy, installed the new officers.

Greater Kansas City Society

Sixteen members were present for the May 2 meeting of the Society of Hospital Pharmacists of Greater Kansas City. The group met at the home of one of the members, Mr. Lyle Willits, at 2:30 in the afternoon.

A highlight of the business discussion was a report from Mr. Lawrence E. Palenshus on the Dallas Science Fair which he attended this year. This was followed by a discussion of the Science Fair to be held in Kansas City during March of next year. The members expressed a wish to participate, and the President appointed the following committee to make plans: Lawrence E. Palenshus, *Chairman,* Ralph M. Fritts, and Lyle Willits. The committee was asked to study details, including costs, help, etc., and present a complete report at the September meeting.

Mississippi Society

On June 22, 1960, the Mississippi Society of Hospital Pharmacists entertained the thirty-one administrators of Mississippi hospitals at a luncheon held in conjunction with the Annual Convention of the Mississippi Hospital Association, at the Buena Vista Hotel, Biloxi, Mississippi. The objective in view was better hospital pharmacy service for the hospitals of Mississippi, the majority of which are under 100 beds and without organized pharmacy service.

Mr. Lewis W. Hauser, Chief Pharmacist from Helena Hospital, Helena, Arkansas, was the guest speaker. Mr. Hauser emphasized the need for the services of a registered pharmacist in every hospital regardless of size, pointing out the dangers involved in the handling of patient drugs by personnel not trained in pharmacology and therapeutics. From the positive approach, Mr. Hauser cited the distinct economic advantage inherent in organized hospital pharmacy service, the economy of purchasing drugs and pharmaceuticals, the control of stock, the just charges to patients, and the equitable margin of gain for the hospital itself. Lastly, Mr. Hauser stated that some workable plan could be devised whereby every hospital could enjoy the benefits of organized pharmacy service, regardless of its size or economic status. It remains only for administrators to seek the advice and guidance of the hospital pharmacist to effect an efficient, economical, and self-rewarding hospital pharmacy service for their hospital.

Mr. Fred McEwen, President of the Mississippi Society of Hospital Pharmacists, spoke to the group, indicating the formulation of a plan for the establishment of a Hospital Pharmacy Consulting Service whereby administrators of the state may seek guidance in setting up hospital pharmacy service in their hospitals. Plans for this consulting service are to be complete by the next meeting in October.

St. Louis Society

The June meeting of the Hospital Pharmacists Association of Greater St. Louis was held at St. Mary's Hospital on June 14. Vice-President Ray Dye presided.

Business transacted included plans for a dinner and installation of officers in September, approval of a deposit in a special savings account, and presentation of a questionnaire on radiopharmaceuticals. Under new business, there was also consideration of the relationship of the organization of Sister pharmacists in St. Louis and the Greater St. Louis group. It was pointed out that the Sisters' group plans to affiliate as a separate organization with the national group.

Suggestions and plans for the program for the coming year were discussed and officers for the new year named. These include John C. Griffin, *President;* Herman Coffman, *Vice-President;* and Emmett Skinner, *Treasurer.* Mr. Robert Newton was named Secretary but will be unable to serve due to a transfer. As a result, the Secretary will be elected by mail ballot prior to September.

As a final business item, plans were discussed for arranging for a seminar in the fall.

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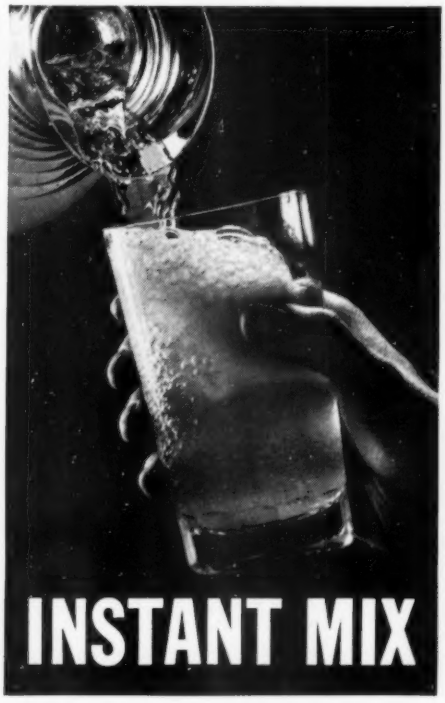

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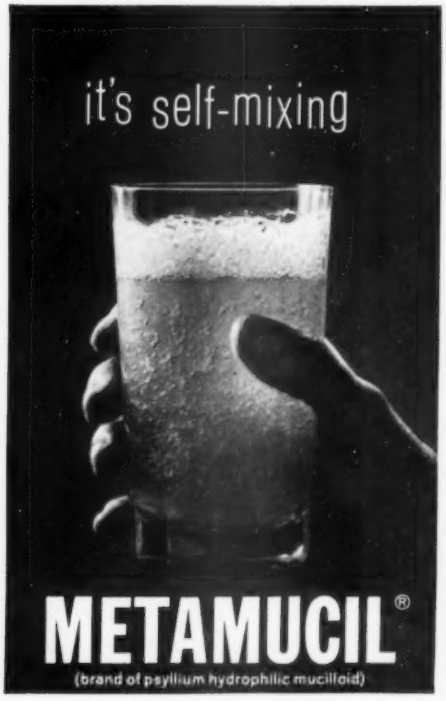

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Greater New York Chapter

In place of the June meeting, the members of the Greater New York Chapter visited the United Nations Headquarters on Thursday, June 23, 1960. The visit consisted of a Guided Tour, attendance at a meeting of the Trusteeship Council then in session, and a dinner served in the delegates' dining room. The members felt that this informal get-together gave them an opportunity to study and observe at first hand some of the problems of other nations.

Officers of the Greater New York Chapter who are serving during 1960 include Sister M. Bernardine, *President,* New York Foundling Hospital, New York; Sister M. Etheldreda, *Vice-President,* St. Mary's Hospital, Brooklyn; Sister M. Angeline, *Corresponding Secretary,* St. Mary's Hospital, Brooklyn; Sister Mary Rita, *Recording Secretary,* Frances Schervier Home and Hospital, New York; and Sister M. Donatus, *Treasurer,* St. Clare's Hospital, New York.

Northeastern New York Society

On Saturday evening, June 25, the Northeastern Society held its Annual Installation Dinner at the Crooked Lake Hotel. Dr. Francis J. O'Brien, Dean of the Albany College of Pharmacy and President of the New York State Board of Pharmacy, was the Toastmaster and installing officer. Mr. Paul A. Freeman of the E. R. Squibb and Sons Company spoke on the topic, "Pharmacists at Work." Mr. Freeman pointed out that even though the medical health team has made progress in the conquest of disease, we should not be satisfied until the progress is turned into complete removal of disease, thus making us a more productive society.

Officers who will serve the Northeastern New York Society during the 1960-61 term include: *President,* Joyce A. Nautel, Columbia Memorial Hospital, Hudson, N. Y.; *Vice-President,* Thomas F. Flynn, Jr., New York State Department of Health, Division of Laboratories and Research, and Albany Hospital, both in Albany, N. Y.; *Treasurer,* Sister Mary Thomas, R.S.M., St. Peter's Hospital, Albany, N. Y., *Corresponding Secretary,* Mr. Leonard Parks, Chief Pharmacist, Putman Memorial Hospital, Bennington, Vermont; and *Recording Secretary,* Janet D. McFadyen, Albany Hospital, Albany, N. Y.

It was also noted that several members of the Northeastern New York Society participated in recent national meetings. Sister Mary Thomas, R.S.M., Chief Pharmacist at St. Peter's Hospital in Albany, and Treasurer of the Northeastern Society, attended the Annual Meeting of the Catholic Hospital Association held in Milwaukee, Wisconsin, from May 31 to June 3.

North Carolina Society

The North Carolina Society of Hospital Pharmacists held its quarterly meeting at Asheville, N. C., Saturday June 25. Business was conducted at the Memorial Mission Hospital Library beginning at 4:00 P.M. Hospital pharmacists throughout the state were in attendance for this annual summer meeting and many took the opportunity to spend the weekend at this mountain vacation resort for relaxation with their families. A variety of committee reports were presented at the business session and recruitment programs for hospital pharmacists were discussed. Appropriation of funds to be donated to the A.Ph.A. Building Fund was authorized and future programing for professional education seminars was considered.

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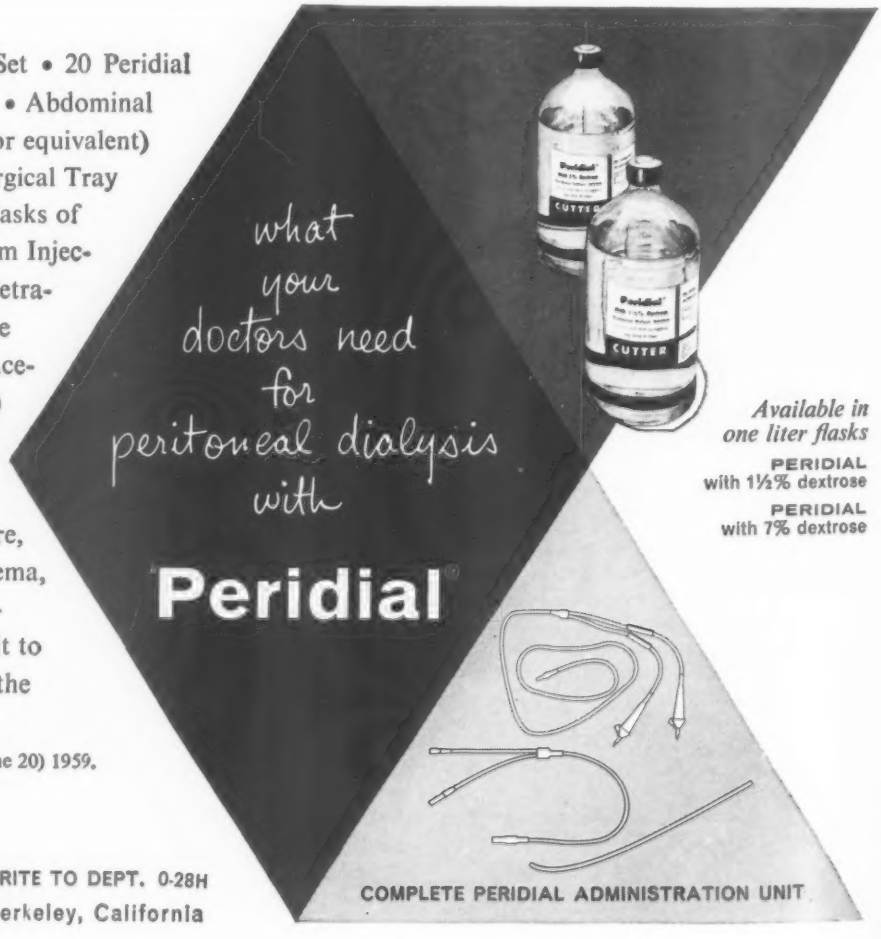
*Maxwell, M. H., *et al.:* J.A.M.A. *170*:917 (June 20) 1959.



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Highlighting the day was a social hour and dinner sponsored by Lederle Laboratories at the Manor Hotel, followed by a panel discussion with participants being composed of prominent representatives of the hospital team. Representing the pharmacists was Mr. I. Thomas Reamer, Chief Pharmacist at Duke Hospital, Durham, N. C.; representing the Administration was Mr. W. W. Lawrence, Administrator at Memorial Mission Hospital, Asheville, N. C.; representing the Medical Staff was Dr. Theodore Raiford, Chief of Staff, Memorial Mission Hospital; and representing the Nursing Staff was Miss Myrtle Barnette, Director of Nurses, Margaret R. Pardee Hospital, Hendersonville, N. C. Various problems of interprofessional relationship were discussed and means of improving hospital pharmacy services were related.

Hospital pharmacists from North Carolina were represented at the Institute on Hospital Pharmacy in Columbus, Ohio. Among those in attendance were Frank Lower, Winston Salem, N. C., Roy Salter, Burlington, N. C., and Rudy Pittman, Smithfield, N. C.

North Dakota Society

The semi-annual spring meeting of the North Dakota Society of Hospital Pharmacists was held at the Grand Pacific Hotel on June 7, 1960. This meeting was held jointly with the North Dakota State Pharmaceutical Association, at which Mr. R. S. Robertson of Seattle, Washington, and president-elect of the American Pharmaceutical Association, was the principal speaker. He discussed the need for stressing professional service and public relations in the field of pharmacy. Mr. A. John Finnie, Director of Pharmacy Service at St. Luke's Hospital in Fargo, North Dakota, participated in a discussion as a representative of hospital pharmacy and reported on the activities of the North Dakota Society.

In the meeting of the North Dakota Society of Hospital Pharmacists, the following items were covered: standing committee reports, nomination of a hospital pharmacist as a possible candidate for the State Board of Pharmacy, science projects for high school students to be sponsored by the North Dakota Society, our responsibility to pharmacy students seeking employment in hospital pharmacies, plans for future meetings, and improving attendance among hospital pharmacists in North Dakota, discussion of proposed regulations with regard to providing pharmacy service in hospitals in North Dakota, publicity, and dues.

Oklahoma Society

The Ninth Annual Meeting of the Oklahoma Society of Hospital Pharmacists was held jointly with the 53rd Annual Convention of the Oklahoma State Pharmaceutical Association.

Each year at this time the OSHP meets for an annual luncheon. During the absence of President Joe R. Davis of the Veterans Administration, Mr. Robert E. McKay, Chairman of the Program Committee and Pharmacist of the U. S. Public Health Service Indian Hospital of Shawnee, Okla., presided over the luncheon and the meeting.

Mr. Gene Jones, of the Whole Drug business in Tulsa, Okla., gave the invocation. Mr. McKay asked all those present (50) to introduce the guest on his/her right to become better acquainted.

After a delightful luncheon, Mr. McKay introduced the principal speaker, Mr. Robert A. Dube, Field Representative of the Prescription Ware Division of the Owens-Illinois Company of Toledo, Ohio. His very timely, informative, and at the same time, enjoyable presentation, "Showmanship in Hospital Pharmacy—The Key to Better Public Relation," was the highlight of the afternoon. This presentation was accompanied by lantern slides, showing mostly prescription departments. He pointed out that no matter which college one had attended, the work in hospital pharmacy with all its duties points all to *better patient care*. He reminded the hospital pharmacists of their duties to the other personnel which makes up the hospital team, including nursing personnel, resident house staff, the attending physicians, etc.

Later during the business session, Mr. E. R. Weaver, Executive Secretary of the Oklahoma State Pharmaceutical Association, who at all times is very much interested in the Oklahoma Society of Hospital Pharmacists, joined us. He presented a gold pin engraved with "25 years" for service in hospital pharmacy to Sister M. Teresa, Secretary of the Oklahoma Society. Other recipients of the pin were Mr. Robert L. Tucker, retired, of the Veterans Administration, and Mrs. Mamie Shilling, pharmacist of Wesley Hospital, Oklahoma City, Okla.

Communications from the national organizations were read and it was agreed to postpone other business to a later date.

On June 4, the Secretary met with Mr. Joe R. Davis, President, and other members to discuss plans for a project. Discussions included plans for revising the Constitution and By-Laws and contributions to special funds.

Virginia Society

At the recent Annual Meeting of the Virginia Society of Hospital Pharmacists, Vernon O. Trygstad, President of the American Society of Hospital Pharmacists, installed the following officers: *President*: Andrew W. Abbitt, Director of Pharmacy Service at Eastern State Hospital; *Vice-President*, Lloyd Dixson, Chief Pharmacist at Kecoughtan V. A. Hospital; and *Secretary*, Justin H. Wilkins, Medical College of Virginia Hospital. Mr. Trygstad also spoke at the annual dinner. Other speakers on the program included Murrill C. Lee, architect, who discussed "Thoughts Behind the Pharmacy Building Program"; Dr. Simon Russi on "Pathology and Pharmacy"; and Dr. Warren Weaver spoke on "Evaluation of New Drugs."

Wisconsin Society

Members of the Wisconsin Society of Hospital Pharmacists met on May 20 at St. Agnes Hospital, Fond du Lac, for the last meeting of the year. Following a luncheon at 2:30, the business session opened at 3:00 P.M. with Vice-President Robert Kubiak presiding in the absence of the President. The hostess, Sister Mary Michael, Chief Pharmacist at St. Anges Hospital, introduced the Administrator, Sister Wilfreda who expressed happiness in having her hospital serve as host for the meeting.

Included on the program was a film entitled "Consultant to Twenty Millions," presented by Mr. Gene O'Hara, District Manager for the Schering Corporation, Milwaukee.

Also included on the program was a presentation by Mr. Pumpian, Secretary of the Wisconsin State Board of Pharmacy. Mr. Pumpian discussed the situation existing in many small hospitals throughout the state regarding handling drugs. It was pointed out that in many instances pharmaceutical service is not provided by legally qualified personnel.

Another part of the program covered the "Wisconsin Poison Control Movement," by Mr. Richard Strommen of the Extension Division of the University of Wisconsin School of Pharmacy. He pointed out that it is felt that every hospital in the state should have a poison control center as a service to the whole hospital. Mr. Strommen volunteered the services of his department to anyone interested in establishing a center.

During the business session, Sister Natalie asked for volunteers to assist with the exhibit which was sponsored by the A.Ph.A. and the ASHP at the Annual Convention of the Catholic Hospital Association in Milwaukee, May 31 - June 2. Also, announcements were made regarding future meetings of interest to hospital pharmacists and various releases from the A.Ph.A. were read.

New officers were announced for the next term including *President*, Sister Mary Natalie, O.S.F., St. Ann Infirmary, Milwaukee; *Vice-President*, George A. Wright, Evangelical Deaconess Hospital, Milwaukee; and *Secretary-Treasurer*, Virginia McVey, Columbia Hospital, Milwaukee.

NEW MEMBERS

The following ASHP members sponsored the New Members listed in this issue of the JOURNAL. *The officers of the* SOCIETY *and the Committee on Membership and Organization appreciate the efforts of the individuals who have encouraged New Members to join the national organizations.*

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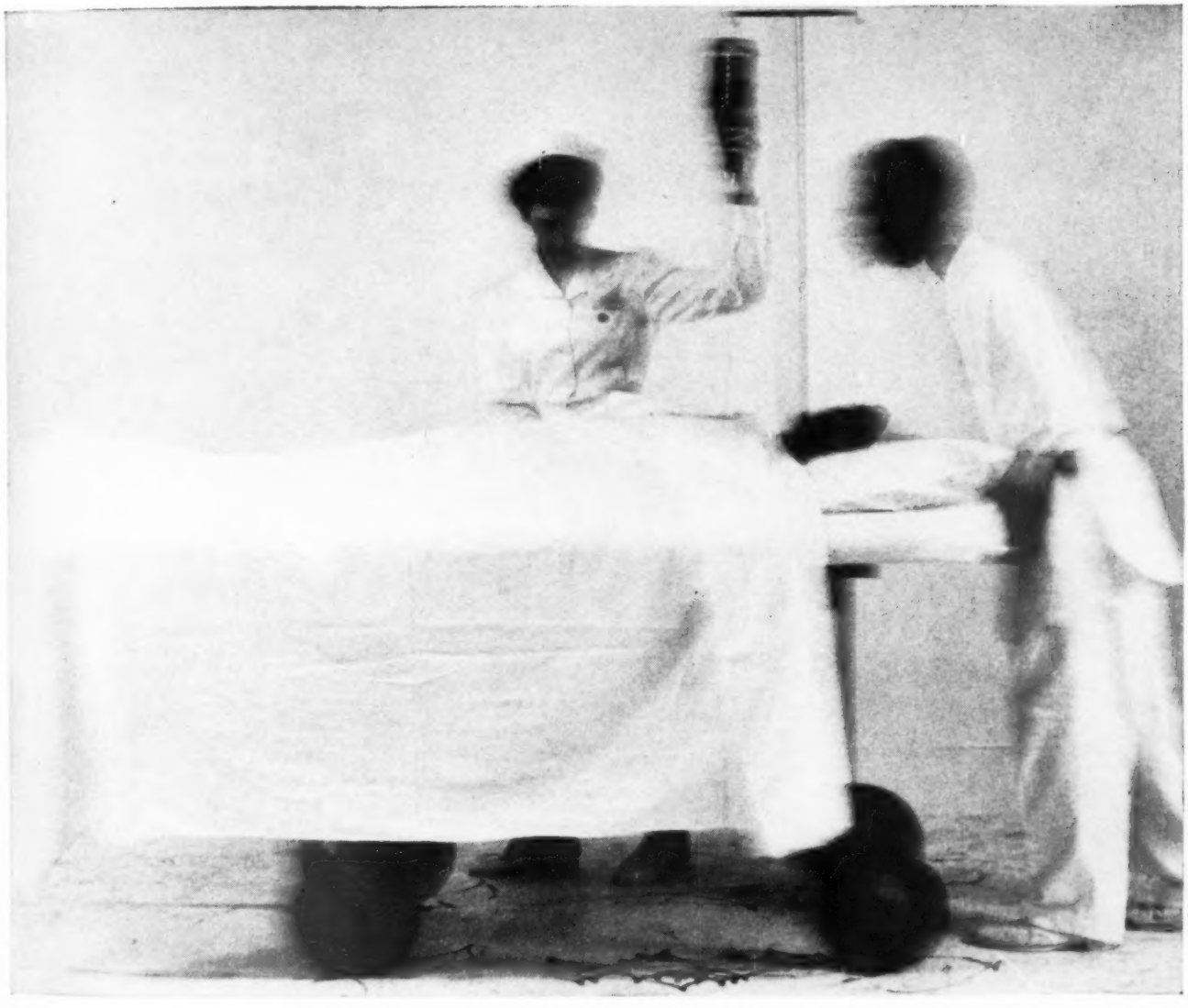

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staph newsletter

SEVENTH OF A SERIES WITH SIGNIFICANT SUGGESTIONS FOR CONTROLLING CROSS INFECTION

EACH month as the many surgical, medical and hospital journals come to my desk, I'm newly aware of the intensive efforts being made to "stop staph" in hospitals all over the world. Pin-pointing any one source for spread of infection seems to have given way to recognition of the many sources of spread—nasal, contact, and airborne—and the importance of reducing staphylococci in the environment to such an extent that they aren't around in sufficient numbers to cause cross infection.

In the March 26, 1960, issue of The Lancet (London), Dr. W. D. Foster reports on an investigation in a 30-bed ward of St. Thomas' Hospital which revealed that when disinfectant mopping was done daily and furniture wet dusted with disinfectant-soaked cloths, cross infection was practically non-existent—even though full isolation precautions were not observed for the eight staph-infected patients in the ward. Relaxation of aseptic cleaning measures immediately brought a rise in infections.

Much discussion goes on in medical and public health journals and at hospital meetings about the continuing need to be aware of the dangers of tuberculosis. Though deaths have decreased phenomenally, incidence is high, and unsuspected infection is an ever current problem. This question from Dr. Carl W. Walter's O.R. Question Box (Hospital Topics, April, 1960) emphasizes some of the dangers.

"Q. Our anesthetists will not allow airways or endotracheal tubes to be autoclaved. Do you approve if they are adequately cleaned?

A. The tubercle bacillus is the most dangerous potential contaminant of anesthesia equipment....Besides protection of the patient from contamination, another concern is protection of personnel. They must be cautioned to immerse soiled equipment in germicide immediately after use, and postpone cleaning until there has been adequate exposure to the germicide."

A new folder on L&F Instrument Germicide is just off the press and contains interesting data on its effectiveness against TB bacilli—*even when dried on instruments.* This germicide penetrates the organism's capsule and destroys it as well as antibiotic resistant Staphylococci, Pseudomonas, fungi and other potentially infectious organisms. We will be glad to send you this new folder and a generous sample of L&F Instrument Germicide. It's ready to use as is, without mixing or diluting.

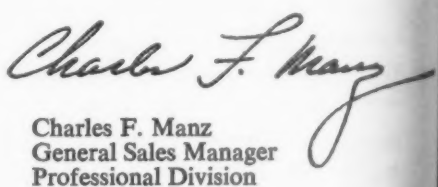
In a study of one year's experience with 29 postoperative wound infections in 984 cases on the orthopedic surgical service, Doctors Tracy and Carr (North Carolina Medical Journal, December, 1959) point up the direct relationship between lengthy procedures and the opportunity for infection. Ten infections were deep, three of these resulting in death. Average delay in recovery in deep infection was 34 days and in superficial infections, 8 days. These surgeons say, "...a long open operation provides ample time for airborne contamination, especially when one considers that the contaminating organisms may already have reached a stage of accelerated growth. With a generation time of 20 to 30 minutes, a small inoculation of organisms (staph) into devitalized tissue or clotting blood can progress to an important focus during a case."

Average operative time was one hour and thirty-five minutes with open hip procedures and lumbosacral fusions taking up to four hours. "Among static objects in the operating suite, five out of six grew hemolytic staphylococci. The airborne spread of organisms was demonstrated by an agar plate exposed in the operating room for one hour, which grew abundant colonies of hemolytic staphylococci."

If you were wondering about the disinfectant activity of Tergisyl® detergent-disinfectant against other infectious organisms besides antibiotic resistant staph, please send for our revised brochure on the new formulation. It is planned for even greater economy in buying and saving in labor. With the new 1:100 recommended dilution, dependable bacteriological control and aseptic detergent action are achieved in one cleaning operation. Rinsing is not even needed. If you would like samples of Tergisyl, as well as the brochure, please don't hesitate to ask for them.

L&F's Tergisyl is the detergent-disinfectant being used at Huggins Hospital in Wolfeboro, N.H., and reported upon by Dr. Ralph Adams, Chief of Surgery, in the April 4, 1959, issue of the Journal of the American Medical Association, after successful control of infection in the O.R. in 300 consecutive cases. With the infection rate still at only .25% after 800 cases, Dr. Adams reported his "zone concept" of O.R. infection control in Surgery, Gynecology and Obstetrics 110:376 March, 1960. Amphyl® was used for blanket disinfection. Reprints of both articles are available. May we send them to you?

Is there an area in your hospital where you find disinfection procedures particularly hard to apply? If so, please accept my invitation to discuss it with us. Although disinfection applies to only one part of the complete infection control program, it is an important one and we just might be able to help. Our research laboratories and technical advisors would be glad to work with you and I, personally, hope you will ask. Please let me hear from you.



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newsletter

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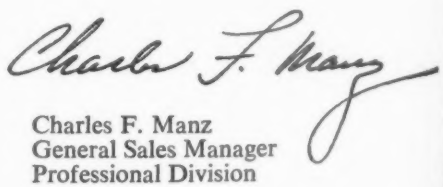

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Dear Sirs:

Comment on Editorial

DEAR SIRS: Allow me to comment on your editorial entitled "Proprietary and Nonproprietary Names for Drugs" which just appeared in the June issue of the AMERICAN JOURNAL OF HOSPITAL PHARMACY. Your statement is the most sensible, succinct, and comprehensive discussion of the subject I have ever seen in print. I would appreciate having a tear sheet of the page for ready reference.

There are two things I like especially about your editorial. First, you placed due and needed emphasis on the professional responsibilities of pharmacists; second, you used the term "nonproprietary" which is not only more correct etymologically but avoids clouding up your discussion with the confusion that enshrouds the term "generic." The latter has been so misused that it is all but completely spoiled for any use in this connection.

LLOYD C. MILLER, *Ph.D.*

Director of Revision
Pharmacopeia of the U.S.
46 Park Avenue
New York 16, N. Y.

Certification Laboratory

DEAR SIRS: I would like to call to the attention of the ASHP membership the interesting item concerning a "Certification Laboratory" which appeared in Francis Chilson's column, a column which I find highly original in ideas, good advice and sometimes amusing, of the *Drug and Comsetic Industry* for April 1959. This item is as follows:

> Some time ago I mentioned the need for a certification laboratory to reduce the amount of time wasted in repetitious control work on identical batches, which are split among several purchasers in the ordinary course of buying chemical supplies. I was thinking of the innumerable times when a batch of chemicals is approved routinely by the chemical manufacturer's control laboratory and then sold piecemeal to many users, each of whom repeats the chemical assays before using the stuff. I, of course, was thinking of the drug manufacturer's problem without realizing that the problem affects individual research people and drug retailers too. Shortly after the note appeared, I got a letter from Dr. William M. Heller of the University of Arkansas Medical Center, in which he wrote:
>
> "As always your column in the November issue of DCI was stimulating. More power to you in your advocacy of a certification system for raw materials.
>
> "If there is anything I, as one of the 3,000 members of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, can do to help, let me know. In the old days we could order our chemicals from Merck or Mallinckrodt and have no doubts. With the need to purchase small lots of newer organic medicinals from firms with which we have had no previous contact we are in a quandary. Often we need these chemicals for a research project if not for patient care. In either case their reliability should be unquestionable.
>
> "Until a certification system is established, if ever, have you any suggestions for the man who has to depend on the supplier's integrity?"

Dr. Heller's letter raises a lot of questions. With the plethora of powerful and often dangerous chemicals of which modern medicines are compounded, one wonders whether the time hasn't come to stop compounding prescriptions, excepting for branded, prepared products, in retail pharmacies. No one can expect the retail pharmacist to check the quality of all the medicinals he buys for compounding purposes. He lacks the training, the time, and the money to pursue such a practice. And, anyway, damn few doctors are capable of writing trustworthy prescriptions, excepting for prepared medicines. But as long as the practice of compounding prescriptions from original medicinals continues, certified medicinals would enormously help those retail pharmacists who do not buy on price and are genuinely interested in the integrity of the materials they employ in compounding prescriptions.

The problem in hospital pharmacies is different from that of retail stores. In the larger hospitals, at least, a lot of clinical work is going on and a lot more experimentation must be done in the hospital pharmacies than in any other type of pharmacy. The position of the hospital pharmacist is similar to that of a pharmaceutical chemist in a research organization. In the latter instance the research man has the facilities and the time to check the materials he uses. In both cases certification would save a lot of time and money. Of course, certification cannot be applied straight across the board because there is no agreement on methods of assaying some products. This is especially true of chemicals of animal origin.

Very often chemicals that pass the routine tests for identity and purity established by their manufacturer contain traces of foreign matter that raise hell with the end use of the chemicals. This foreign matter may originate in the equipment and handling methods of the chemical manufacturer, and go undetected by his control chemists whose sole purpose is to make certain that the product sample conforms to the specifications established for it. I've run into hundreds of cases of stray contaminants. But if we had a certification laboratory, its procedures would be set up from the point of view of the chemical user and not the chemical makers and these contaminants would very likely be detected. One thing is certain: if we had a certification laboratory, an army of chemists could be transferred to more important work.

EVLYN GRAY SCOTT, *Director of Pharmacy Service*
St. Luke's Hospital
Cleveland Ohio

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editorial

by DON E. FRANCKE

HOPE For Humanity

► OF ALL THE SOURCES WHICH HAVE FED the capricious stream of international collaboration during the past century, none is more potent than man's quest for health. Nations may not be able to stomach each other's politics but what is good medicine in the East is swallowed with equal ease in the West.

Health Opportunity for People Everywhere (HOPE) is one of the most imaginative privately sponsored projects yet devised to carry to the newly developed countries the medical knowledge and skills they so sorely need.

Project HOPE, a people-to-people program initiated at the suggestion of The President of the United States, is headed by Dr. William B. Walsh, noted internist and heart specialist of Washington, D. C. HOPE will send a floating medical training center to Southeast Asia during its first year of operation. The S. S. HOPE, formerly a Navy hospital ship now on loan from the U. S. government, is a 15,000-ton vessel with 230 beds. The permanent staff of the S. S. HOPE will include top specialists in the key fields of medicine who have volunteered to serve on a rotating basis for tours of four months. Part of the health teams will work on shipboard while part will be assigned inland, to mobile teams, where they will work with their counterparts of the newly developing countries to enable them to gain modern techniques and latest medical knowledge.

Thus, HOPE is primarily a teaching program, although, as in the modern teaching hospital, treatment will be necessarily involved. Instruction will also take the form of classroom lectures and discussions, supplemented by movies and film strips. Teaching is to be stressed because it will result in a more enduring effect on local health conditions than would attempts limited to widespread treatment. There are too many millions in the need of treatment for such a relatively small project to have broad impact in actually curing disease. Concentration on teaching will enable HOPE personnel to help upgrade local medical people in their ability to diagnose and treat—and these, in turn, will be able to teach others. As a result the impact of HOPE will keep expanding constantly.

First stop of the S. S. HOPE is Indonesia, a country of some 3,000 islands, where the ratio of physicians to the population is only about one-hundreth of that in the United States and where assistance with health problems is desperately needed. After six or seven months in Indonesia, the ship will go to Viet Nam for several months. Invitations have also been received from Korea, Okinawa and Pakistan.

Pharmacists also have an opportunity to participate in Project HOPE on a staff or volunteer basis. Because of the nature of the project, any remuneration would be considered as a token payment and, thus, the pharmacists selected must have high motivation for service. The pharmacists will be expected also to participate in the teaching program and must have the necessary skills and experiences in this area. They should have rather extensive knowledge and experience in broad areas of pharmacy practice, in addition to dispensing. More than 1500 physicans, nurses and other medical personnel have sought assignments with the project. Many of the applicants have top reputations in their field, well-paying practices, high-paying jobs. With Project HOPE, their hours will be long, the pay short, the weather hot. But the personal rewards will be great. Hospital pharmacists interested in obtaining further information relative to their participation in this project may write to Dr. William B. Walsh, Project HOPE, Box 9808, Washington 15, D. C.

The ASHP is interested in making the benefits of good pharmaceutical practice available to people everywhere. While this objective has practical limitations, it is especially fitting that the SOCIETY should cooperate in a project organized on a people-to-people basis. Need of medical care and the training of all types of health workers is unbelieveably great in many poverty-stricken countries. A disease-ridden people cannot break the vicious cycle of poverty, hunger, illness, and dispair. With a little help, however, the cycle can be broken and millions can gain new hope. President Trygstad has demonstrated the interest of the ASHP by presenting a copy of the *American Hospital Formulary Service* to Project HOPE and he has encouraged members of ASHP and other pharmacists to support this humanitarian effort.

HOPE for humanity deserves the active support of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS and of pharmacists everywhere.

MUTUAL AREAS OF COOPERATION between pharmacy and nursing

by GEORGIANA OCHS

► GOOD MANNERS AND RESPECT FOR THE WORK OF others promote good work relationships. Because of work pressures, all of us are sometimes neglectful of the needs of other departments.

Nurses are concerned about the role they play in interdepartmental relationships. Since a role is a relationship one accepts with his associates whose characteristic work tasks are many times unlike his own, each group in the relationship develops expectations which it anticipates the other will fill. These expectations involve responsibilities and functions.[1]

To avoid conflicts, workers in interdependent services need (1) to know exactly what is expected of them and (2) to be able to perform to the satisfaction of one another. This ideal situation rarely develops in the hospital.

Coordinating Function of the Nurse

Hospitals are made up of groups of specialists. Each of us can know his own work area and its problems better than any one else in the hospital, but we can no longer have broad knowledge of the work of another,

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nor of his problems. The complex organization of the modern hospital, and hospital bigness have become dividing forces which block communications and make them impersonal. It is said that a marked change in climate takes place in the hospital at about the 100 bed size.[2]

Services to the patient and many skills for his care must come to him through the nurse. The nurse provides the channel to the patient; she is the applier and the utilizer of services for him; she becomes frequently the buffer between and among services. The nurse must attempt to personalize service to the patient and to bring together all aspects of care that specialization is fragmenting more and more.

This coordinating function of the nurse in the hospital gives her prestige and authority in an organization where nursing service is always the largest service in terms of numerical weight. Nursing personnel is the largest employed group in the hospital. Nurses have continuous access to patients and to physicians and are able to influence them. This increases the nurses' power in the organization. The position in which the nurse finds herself and in which nursing service finds itself, sometimes produces hostility toward and criticism of nursing service by other hospital departments that are frustrated in their attempts to reach the patient through the nurse or through her designate. Nurses themselves fail to recognize and accept this position in which they are placed. Nurses whose conceptual skills are limited feel that other people in the hospital make unreasonable demands of nurses and that nursing service is criticized unduly.

Qualities of Nursing

Nursing has a number of qualities that differentiate it from other hospital services.[3] These characteristics need to be understood by other hospital departments because they affect operation of other departments.

One quality that differentiates nursing from other hospital services is the continuousness of service. Nursing service never closes. The normal operations covers a twenty-four hour day, and a seven day week. All who work in the hospital know the constancy of nursing service, but not all understand the strain this places upon human resources. The normal work week is a 40 hour one for hospital personnel. The patient and his needs are with us for 168 hours of each week. We are all part-time workers in relation to the time span of patient care needs.

The staffing problem is further complicated in nursing by the part-time worker. In some hospital nursing services, as much as 30 percent of the nursing staff may be part-time nurses who work as infrequently as one day per week, one night per week, or a few days every other week. Communication with this group, which must be of a special design, is seldom effective.

The burden falls upon the most stable element of the nursing staff which is the head nurse group. Head nurses administer the nursing service program and aspects of other hospital programs. Head nurses are held responsible for communication and coordination techniques. For this reason, there are nurses today who believe the head nurse position is not tenantable.

Diversity of Function

Another unique characteristic of nursing service is the diversity of function which requires numerous skills. This diversity of tasks is brought about by the diversity of patient needs, and by nursing's absorption of the functions of others in the hospital. The California State Nurses' Association conducted a study of hospital nursing activities in 1953. This study investigated a task list of 439 nursing functions. The findings of this study filled two volumes, one of which contained 400 pages.

In the same year a similiar study in the state of Kansas of the functions of 90 nurses in 23 small hospitals reported a total of 384 tasks for nurses, and management consultants who conducted the study observed nurses in 98 more tasks which nurses failed to report.

People who work in the hospital soon learn that the nurse feels she is expected to be all things to all people, but not all people understand the way in which this diversity of function stretches skills and resources in nursing services. Such diversity of tasks in nursing services has many implications for inservice .education which is time consuming and costly.

Urgency

Another characteristic of nursing which differentiates it from other hospital services is the urgency in nursing situations. The patient is the most dynamic person in the hospital. Changes in condition of patients can come about with explosive suddenness and are difficult to predict and to control. It is sometimes necessary to direct all unit resources to the care of one individual for a long period of time and other tasks are delayed.

Pressure of Social Tensions

Still another unique quality of nursing service is the intensity of the social atmosphere on the nursing unit. This cannot be matched elsewhere in the hospital. There is constant traffic on the nursing unit. In addition to the fixed staff, many people who have an episodical function on the unit come and go. All come with demands to make and to be met. The nurse deals with the emotions of the patient, of the family, of the community, of the physicians, of her subordinates, of her peers, of her superiors, of other departments and with her own emotions. These tensions affect administration

of the nursing unit and are communicated to other hospital departments where they have impacts. This situation in nursing is not likely to change.

Educative Role of Pharmacist

Personnel in nursing service appear to have different sets of expectations for pharmacy services and to see the professional pharmacist in several roles. I asked student nurses, head nurses and a unit secretary what they expected from a pharmacy service in the hospital. The students said immediately, "they know all about new drugs." The student placed the pharmacist in his educative role and considered him a trusted source of information.

I asked a small group of experienced head nurses what they expected of the pharmacy. One head nurse answered immediately, "accuracy." The group then elaborated upon this. Head nurses stressed the labeling of drugs, procedures for the control of narcotics, warnings about use of very potent drugs, mixing and diluting of drugs, evaluating orders and dosage checks. The nurses in administrative positions were concerned with safety factors. Head nurses visualized the pharmacist as a protector of patients, of the nurse and of the physician, and expected him to provide protection for all three groups in the administration of drugs.[4]

Pharmacist's Clinical Role

In our hospital unit secretaries process physicians' orders, prepare pharmacy requests, prepare medicine cards and maintain the nurses' reference card. The secretary has many contacts with the pharmacy; she prepares most of the day-time requests for drugs. I asked a unit secretary what she believed the function of the pharmacist was and she replied "the pharmacist carries out the physicians' orders by supplying the drug at the right time and in the right amount." This secretary emphasized the pharmacist's clinical role. The secretary said the pharmacist participates in therapy beyond a helping role because she hears telephone conversations between the pharmacist and the physician, and between the pharmacist and the nurse who speaks for the physician. The secretary placed the pharmacist at the top of the hospital hierarchy and said "it is medicine that gets the patient well."

The nurse appears to be compulsive about administration of medications, more so than she is about other aspects of care. Some nurses say the medication comes first with them because it comes first with the patient and appears to come first with many physicians. I asked the secretary if the nurses' attitude had rubbed off on her. This she denied. The secretary said she believed, on the basis of her observation, that efficient pharmacy service shortened hospital stay. This worker believes the speed with which medication reaches the unit has a direct relation to the length of hospital stay.

Expectation from Pharmacy Service

Nurses have many expectations for hospital pharmacy services. The extent to which these expectations can be met will depend upon the philosophy of the pharmacy department, and the degree to which this service is able to and willing to extend itself. I have listed a number of such expectations. This is the system which operates in our own hospital. It is time-consuming for the pharmacy, requires many personal contacts and many telephone calls, and it is effective.

Nurses expect hospital pharmacy service:

1. To establish policies for ordering of drugs that are practical for accomplishment by nursing service.
2. To use a system that conserves nursing time and effort.
3. To establish policies and procedures for the control of narcotics.
4. To provide for continuity of pharmacy service in the absence of a pharmacist through a system that is safe for the patient, safe for the nurse, and economical in the use of nursing time.
5. To provide a pickup and delivery service.
6. To provide for immediate delivery of drugs needed in emergencies.
7. To provide on the unit reserve supplies of frequently used items and items for emergency use.
8. To maintain control of stock items by routine checks for amounts, conditions of labels, etc.
9. To investigate any questionable order.
10. To check dosage.
11. To label completely any item dispensed by indicating on the label any equivalent dispensed, any difference in size of unit dispensed, and complete instructions for administration.
12. To dilute and mix drugs.
13. To calculate dosage from solutions and supply instructions for administration.
14. To warn nurses about drugs of unusual potency dispensed and not commonly used.
15. To dispose of hazardous items such as empty aerosol cans, empty ether cans, empty nitrogen mustard vials.
16. To inform the nursing unit when there will be an unusual delay in procuring a drug.
17. To caution nurses about the use of very expensive drugs to prevent any waste.
18. To provide expert guidance in the construction of nursing procedures which require the use of bactericides and sterilizing agents.
19. To instruct nurses on the storage of drugs to prevent deterioration and loss.
20. To provide expert opinion in formulation of nursing policy as it relates to the role of the nurse in intravenous therapy.

21. To provide nursing service with information about acceptable routes for administration of injectable drugs.

22. To provide a hospital formulary service which can be used and understood by nurses.

23. To supply information to individual nurses about drugs and specific drug therapy.

24. To assist in the inservice educational program for nursing service personnel.

Expectations from Nursing Service

The pharmacy department is entitled to a set of expectations which it can anticipate nursing service will fill. I have listed expectations which I believe hospital pharmacy services have for nursing service.

Hospital pharmacists expect hospital nursing personnel:

1. To observe policies of the department and to consult them when in doubt.

2. To notify the department of the patients' needs promptly and at the time when the service can be provided, if this is possible.

3. To handle problems that arise promptly.

5. To interrupt work if necessary to make it possible for the pharmacy to function.

6. To be personally responsible for obtaining information about drugs administered.

7. To follow approved, established procedures in the administration of drugs.

8. To be ever mindful of the legal aspects in the handling of narcotics.

9. To avoid the waste of drugs by careful handling.

10. To be economical in the use of accessible supplies as well as those regulated by individual prescriptions.

11. To be aware of all implications in the self-administration of drugs.

12. To accomplish any inventories needed by the service at the designated time.

13. To provide proper storage of drugs to avoid overstocking and waste.

14. To return unused drugs to the pharmacy promptly.

15. To return drugs to the pharmacy for relabeling.

16. To act as a liaison between the pharmacist and the physician in solving specific therapy problems.

17. To assist in interpreting pharmacy policy to the physicians.

Nursing-Pharmacy Relationships

Cooperative planning through frequent consultation of heads of the departments will establish policies and procedures for overlapping functions. People who work in the departments usually find the practical solutions to the mechanical problems.

The lateral relationship of the heads of the service is most important. The chief of the service always sets the climate; his attitude is reflected in that of the people who work with him.

After policies and procedures are established, the most difficult aspect of administration begins which is maintaining validity of established and approved procedure. This is a continuous responsibility of both services.

If we are to fulfill one another's expectations in hospital nursing service and hospital pharmacy service practices, mutual cooperation must come about through:

1. A mutual trust in the moral strength of each other's service. We need to respect each other.

2. An inherent desire to apply the legal principles that underlie the professional practice of both groups.[5]

3. An appreciation of the direct and indirect contribution each service makes to the care of the patient.

4. A comprehension of, and an acceptance of interdependence, and communication of this to all personnel. Nursing has more contacts with pharmacy than with any other service. We cannot get along without each other.

5. A recognition of the need for each other to carry out his function in an organized way.

6. An understanding of the hazard to the patient in drug therapy which necessitates inflexible rules to provide for safety.

> For a hospital is of all social institutions, the one in which perhaps the greatest mixture of emotions, the most incompatible ambitions, and the most vexous vested interests are thrown together. It is a dinner party to which incompatible guests have been invited, so much so that the dinner table is often in danger of being upset.
>
> John Langdon Davies,[7]
> Westminister Hospital, 1719-1948

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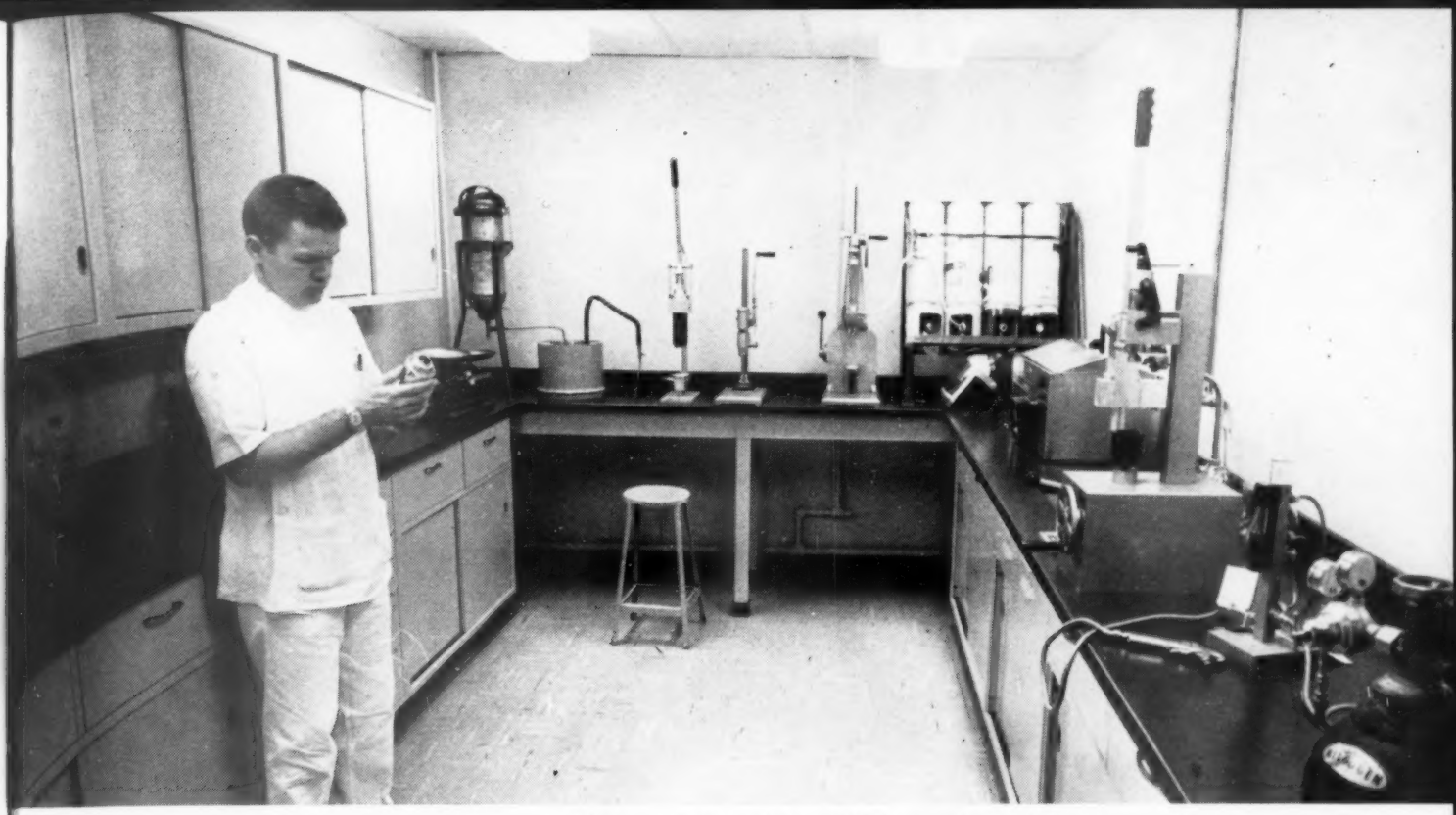

Figure 1. Left to right: cold-fill apparatus, bottle and can crimper, pressure-fill apparatus, propellants, water bath and nitrogen gassing unit

AEROSOL SPACE DEODORANTS
for hospital use

by WILLIAM M. HENDERSON *and* SEYMOUR M. BLAUG

► AT THE PRESENT TIME, DEODORANT PRODUCTS fall into three classes. The wick-type liquid deodorant relies upon the immersion of cotton or wool wicks or swabs into the liquid. The deodorant passes into the air by slow evaporation from the saturated wick. The rate of evaporation is dependent on physical factors such as the vapor pressure of the liquid, temperature of the air, and any air currents present. This method is not too effective as its efficacy is dependent on many uncontrollable variable factors.

The liquid product with a spray dispensing closure is the second type of deodorant form. Here again the efficiency of the product is quite variable, depending on the physical factors present. However, it represents an improvement over the wick-type in that it puts more deodorant into the air per unit of time and makes an attempt to disperse it.

Particle size has been found to have a direct bearing on the efficacy of a deodorant.[1,2] For example, if a formulation in aerosol form is sprayed into the air, it is considerably more effective than the same formulation in identical quantity sprayed into the air from a spray-top bottle. Since the surface area of a spherical droplet is directly proportional to the square of its radius, the difference in effect is probably due to the enormous area of the droplet-air interface of the pressure-propelled deodorant as compared to the area of the droplet-air interface obtained from the spray-top bottle. Kilgore's study of substituted acrylic acid esters as space deodorants supports this conclusion.[2]

Pressurized Aerosol

The third deodorant product form is the pressurized package or aerosol. From the previous statements, it is evident that per unit-volume of deodorant composition employed, the aerosol form is by far the most efficient. This efficiency depends on the excellent utilization of the deodorant composition which in turn is due to the small particle size and large surface area of the deodorant sprayed. "Flashing" (sudden vaporization) of the propellant upon hitting the atmosphere further helps to reduce the particle size and increase the effec-

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tiveness. Small particles settle at a slower rate than large particles, hence a more prolonged action is obtained from the pressurized product than from the ordinary spray-type product. There are other subsidiary factors which will be discussed at another point which also favorably influence the efficiency of the aerosol deodorant form.

Classification of Deodorant Compounds

Deodorant compounds are usually divided into four classes, according to their mechanism of action. They are: (1) aromatics, (2) local anesthetics, (3) glycols, and (4) fixatives.

Aromatic Deodorants

The aromatic deodorants consist usually of an oil base such as Stoddard's solvent with the addition of many and various aromatic oils, solids, etc., which provide almost any scent desired. These formulations are based on the presumption that they have a longer and stronger effect on the olfactory sensibilities of a person than the disagreeable odor. This is not a sound basis for formulation and certainly not a true type of deodorant by definition. The mechanism is based on the substitution of a stronger odor in an attempt to "override" the original undesirable odor. In addition, highly concentrated aromatics can become somewhat disagreeable. Here again, subjective perception and classification of odor by various persons will give rise to widely-varying opinions as to efficacy and residual odor. What may be a pleasant odor to one person may be nauseating to another.

Local Anesthetics

The second type of deodorant compounds are those that produce a short-lived local anesthetic effect upon the olfactory sensory nerve endings in the nares. It is obvious that no odor will be detected if the olfactory nerve endings are temporarily paralyzed. It is just as obvious that the use of this type of deodorant can have adverse effects. If this must be the predication and measure of a deodorant's efficiency, then it is a poor basis for the rational formulation of a product. The best example of this type of deodorant is formaldehyde. In all fairness, formaldehyde does possess some odor destroying properties, however, it enjoys the dubious distinction of being a primary irritant and can also react with the material common to clothing, etc.

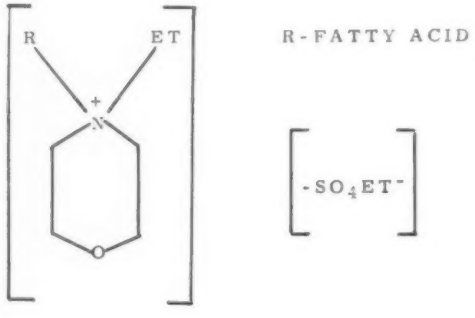
Polyglycols

The third type of deodorant compounds are the lower polyglycols. These include triethylene glycol, diethylene glycol, dipropylene glycol, hexylene glycol, etc. The deodorant action of the glycols is probably due to the solvent action of the air-borne glycol droplets on the odorous materials in the air. In addition, the primary hydroxyl groups and ether linkages in some glycols are sufficiently reactive to form hydrogen bonds or nonodorous condensation products with the odoriferous entities present in the air. The glycols also possess a moderate degree of bacteriostatic activity when sprayed or vaporized by heat into the air against air-borne bacteria, specifically gram-positive organisms.[3,4,5] Lester has discussed the mechanism of action of some of the glycols.[5] The glycol deodorant systems generally contain triethylene glycol. Under ideal conditions of temperature and humidity, vaporized triethylene glycol in a concentration of from 2 to 5 micrograms per liter of air, will render the atmosphere almost sterile in three to four minutes.[4,5] The glycol deodorant systems generally contain aromatics, the rationale for the inclusion of the aromatics presumably being that the public is convinced that nothing which is odorless *per se* is capable of destroying odor. This is no doubt due to the preponderance of aromatic deodorant aerosols now on the market.

Fixation Types

The fourth and probably most important class of deodorant compounds are the fixation types. This class of compounds can be divided into two groups. The first group consists of the cationic surfactant type deodorants. Several different quaternary compounds at present share the property of "fixing" or neutralizing disagreeable odors.

Quaternary morpholinium alkyl sulfates have been recommended as air deodorants[6] in combination with a partial ester of a polyhydric alcohol and a higher fatty acid as a solubilizing agent. The solubilizing agent is required to dissolve the quarternary compound in the propellant. N-Soya-N-ethyl morpholinium ethyl sulfate is commercially available as "G-271" from the Atlas Powder Company.

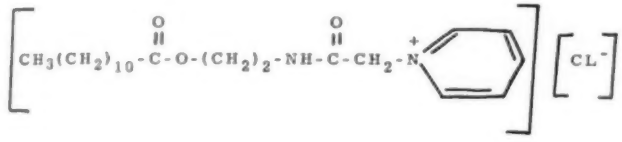


QUATERNARY MORPHOLINIUM ALKYL SULFATE

(Product of the Atlas Powder Company, Wilmington, Delaware.)

Another quaternary compound, "Emcol E- 607," is

available commercially as a deodorant compound.[7] It is a substituted fatty acid ester of pyridinium chloride, N-(lauryl-colaminoformyl-methyl)-pyridinium chloride. The exact mode of action of these two quarternaries is not fully understood. However, it is known that these materials do not mask odor; they destroy the odoriferous material present in the atmosphere. The mechanism of deodorant action is presumed to be a chemical reaction involving the quaternary nitrogen and reactive components of the odoriferous materials such as sulfhydryl groups, skatol rings, amine groups, etc.[2]



EMCOL E-607

(Product of the Emulsol Chemical Corporation, Chicago)

The second group of chemical fixatives which possess deodorizing properties are certain unsaturated short chain acids esterified with various fatty alcohols.[2,8] The only one of these commercially available at the present time is the lauryl ester of methacrylic acid which is patented under the tradename of "Metazene."[2] The mode of action here is also presumed to be chemical reaction, in this case involving the double bond on the end of the parent acid moiety of the ester molecule. There is also the carboxyl group present as there is on the cyclic quaternaries discussed. However, there is no evidence that the carboxyl groups present in the "fixative" type of deodorants take part in the mechanism of "fixation." Another possible mechanism of action may be attributed to an electrostatic attraction between the minute deodorant droplets sprayed into the air and the odoriferous material.[5]

METAZENE

(Product of Motomco, Incorporated, Clark, New Jersey)

Aerosol Laboratory

The primary purpose of this study was to establish an aerosol laboratory and investigate its applicability to a small scale production facility in a hospital pharmacy. Space deodorants were studied because of their relatively widespread use in hospitals and knowledge gained from their study can be applied to other pharmaceutical products such as spray bandages, body and hand lotions, inhalations, etc.

Experimental

In this study, trichlorofluoromethane ("Ucon-11") and dichlorodifluoromethane ("Ucon-12") were utilized as the propellant mixture (50/50). Propellant 12 was employed as the primary propellant and type 11 was used as the vapor pressure depressant. Since all formulations studied were anhydrous, the possibility of propellant hydrolysis was minimized. The 50/50 ratio of propellants in the mixture was chosen for two reasons: this ratio of propellants 11 and 12 yields a vapor pressure of approximately 37.5 p.s.i.g. at 21°C. which produces a large spray plume with the formulations studied; and the presence of propellant 11 (v.p. of 13.4 p.s.i.a. at 21°C.) made possible a filling procedure involving a combination of the cold fill and pressure fill methods. This procedure reduced the possibility of pressure overage due to entrapped air[9] because of the flushing of air from the container by the partial vaporization of propellant 11 prior to crimping the valve on the container.

The physical and chemical properties of the common halogenated propellants have been investigated exhaustively.[10] The hazards of toxicity from use in closed areas and/or in the presence of flame or hot surfaces has also been reported.[11]

A non-polar solvent, mineral oil, was added to the final formulations in order to prolong the deodorant activity[2] of the sprayed formulation. Mineral oil apparently prevents the rapid loss of the minute deodorant aerosol droplets in the atmosphere without altering its deodorant properties.

The deodorant formulations studied impart little or no odor to the atmosphere. Testing of these formulations in the hospital wards indicated that many users are conditioned by household use of space deodorants to expect an aromatic odor in the air after using a space deodorant. For this reason, several different aromatics were incorporated in the deodorant formulations studied. It was felt that this would make available to the hospital a basic odorless or nearly odorless space deodorant which could easily be prepared as such, or perfumed with any of the aromatics tested.

A small orifice valve and actuator were used in this study in order to produce droplets of small diameter. It was found that a wide angle spray pattern and small droplet size minimized the rapid settling or deposit of the droplets on a surface.

Materials

Ucon[1] brand of trichlorofluoromethane (Type 11) and dichlorodifluoromethane (Type 12) propellants. "Metazene" concentrate, 80 percent in deodorized kerosene; N-(lauryl-colaminoformyl-methyl)-pyridium chloride ("Emcol E-607"); Liquid Petrolatum, U.S.P.;

[1]Ucon, from Union Carbide Chemicals Co., New York, N. Y.

Anhydrous Ethanol, N.F.; spice, evergreen, and floral bouquet perfume oils[2]; and deodorized kerosene.

Container and Valve Assembly

Crown[3] seamless six ounce 2-P containers, 0.5 lb. tinplate body lacquered inside and white outside; Fischer Porter[4] Compatibility Tubes, six ounce; Precision[5] NN valve with nylon stem having 0.018" orifice and mounted in a tinplate cup; Precision actuator No. 10014, polyethylene press button with an 0.018" orifice.

Filling and Testing Equipment

Foresman[6] Liquified Gas Manipulator, model No. 38; Mojonnier[7] can crimper, model No. 704LCM; Labline[8] water bath with stainless steel gable; J. P. Marsh combination type pressure gauge, 0-150 p.s.i.g. pressure, and 0-30 p.s.i.g. vacuum, both scales in 3 lb. graduations. The aerosol laboratory and physical layout is shown in Figure 1.

Filling and Formulation Procedure

All formulations were filled by a combination of cold fill and pressure fill. The active ingredients, co-solvents, and perfumes were mixed with the Type 11 propellant, previously chilled to 4°C., and filled into the containers by weight. The containers were allowed to stand two minutes before crimping on the valve assembly to allow the Type 11 propellant to vaporize sufficiently to purge the residual air from the container. The containers were filled with the Type 12 propellant after the valves were crimped in place. Sufficient propellant was added to bring the total weight of the formulation to 100 grams. All the cans were placed in a constant temperature water bath adjusted to 55°C. ± 1° for 15 minutes in order to test for leaking cans.

Nineteen formulations were prepared using various combinations of "Metazene," "Emcol E-607," perfume oils, co-solvents, and propellants. Two formulations were selected for evaluation by hospital personnel on the wards. Other formulations were eliminated because of lack of solubility of some of the ingredients in the propellant mixture, unsatisfactory spray pattern, or poor delivery rate. The two formulations selected are shown below.

Formulation A	Percent by Weight
"Metazene," 80% concentrate	4.0
Liquid Petrolatum, U.S.P.	5.0
Trichlorofluoromethane/Dichlorodifluoromethane (50/50)	91.0
Vapor pressure at 22°C.:	38 p.s.i.g.
Flammability (12):	nonflammable
Delivery rate (13):	1.24 Gm./sec.

Formulation B	Percent by Weight
"Emcol E-607"	0.5
Liquid Petrolatum, U.S.P.	5.0
Anhydrous Ethanol, N.F.	5.0
Trichlorofluoromethane/Dichlorodifluoromethane (50:50)	89.5
Vapor pressure at 22°C.:	40 p.s.i.g.
Delivery rate:	1.20 Gm./sec.
Flammability:	nonflammable

These formulations were also prepared using the various perfume oils previous listed. One-half (0.5) percent by weight of the perfume oil was used in each formulation.

Testing Procedures

In addition to filling the above formulations into metal containers, three Fischer-Porter Pyrex compatibility tubes were filled with each formulation in order to observe any visible signs of separation or color change. The flasks were stored at ambient temperature and observed for eight weeks. Two cans of each formulation were stored at 4°C., ambient temperature, and at 55°C. for eight weeks. Each set of containers was evaluated weekly for changes in vapor pressure using a Marsh combination pressure gauge. The pressure remained constant at each temperature: *i.e.*, 23 p.s.i.g. at 4°C., 38-40 p.s.i.g. at 22°C., and 80-84 p.s.i.g. at 55°C.

Changes in the spray pattern were evaluated visually by noting the length and the width of the spray cone and by spraying each formulation on a hard paper surface from a standard distance and noting the amount of "running." No changes were noted in the spray pattern of each formulation over the test period. This was expected in view of the constant vapor pressure over this test period.

Changes in the odor were evaluated qualitatively by spraying each formulation into a confined space such as a large bell jar. No change was noted in the odor of formulation A. However, after four weeks, a pyridine odor was noted with formulation B. A qualitative test with bromine and carbon tetrachloride confirmed the presence of pyridine.

Flammability of the pressurized formulations was determined according to the flame projection test of

[2]Floral perfume oils, from Magnus, Mabee & Reynard, Inc., New York, N. Y.
[3]Crown containers, from Crown Cork & Seal Co., St. Louis, Mo.
[4]Compatibility tubes, from Fischer & Porter Co., Hatboro, Pa.
[5]N N valve, from Precision Valve Corporation, Yonkers, N. Y.
[6]Liquid gas manipulator, from Robert A. Foresman, Jr., Philadelphia, Pa.
[7]Can crimper, from Mojonnier Associates, Franklin Park, Ill.
[8]Water bath, from Labline, Inc., Chicago, Ill.

the Chemical Specialties Manufacturers Association.[12] This test indicates how far a flame will extend beyond a microburner if the spray from a pressurized container is directed through the flame under standardized conditions. Neither formulation produced more than the normal bending of the flame, nor was any flash-back detected.

Delivery rate[13] was determined for each formulation at ambient temperature by activating the valve for five seconds, then weighing the container to the nearest 0.1 gram. The valve was then activated for a period of 10 seconds and the container again weighed. The delivery rate is reported in grams per second. Duplicate tests were made on each container. The delivery rate is calculated as follows:

$$\text{Delivery Rate (Gm./sec.)} = \frac{\text{weight loss in grams}}{10}$$

At the end of the eight-week test period, the containers stored at each temperature were punctured and cut apart. The valves were separated from the valve cups and all the parts of the container and valve assembly were examined macroscopically for any corrosion or pitting. The diameter of the valve eductor tubes from each container was measured with an Ames Thickness Measurer, model No. 25, and compared with the diameter of the eductor tube taken from an empty container. No corrosion or pitting occurred in any of the containers or valves. No measurable change was detected in the eductor tubes taken from the containers stored at 4°C. and at ambient temperature. There was a slight increase (0.005" to 0.01") in the diameter of the tubes taken from the containers stored at 55°C. This very slight swelling was less than anticipated.[14]

Summary

The aerosol or self-pressurized package form has been discussed in relation to its utilization for delivery of space deodorants. Space deodorants were classified as to type and the rationale for the choice of the chemically-reactive or "fixative" type discussed. The equipment and the physical plant used in the formulation of the aerosol products has been mentioned and pictured in Figure 1.

Deodorant formulations A and B, without aromatics, were manufactured in trial lots and subjected to clinical trial on several of the surgical wards of the University of Iowa General Hospital by staff nurses on each ward. The formulations were labeled as "Space Deodorant A" and "Space Deodorant B." Questionnaires were issued with each unit of formulation. The majority of nurses preferred the "Metazene" deodorant (formulation A) to the quaternary deodorant (formulation B). Factors specifically mentioned were the ease of use, quickness and completeness of efficacy, and the lack of residual odor. The slight transient odor of the aerosol *per se* was mentioned, but was not in the form of an objection as such. Mention of the deodorant odor *per se* would seem to be an indication that persons are conditioned to expect an aromatic odor in an aerosol space deodorant. This was not an unexpected factor and was the prime reason that the trial deodorants were formulated unscented. However, the aromatics previously mentioned (spice, evergreen, and floral bouquet) are suitable for addition to this type of deodorant should odor variations be desired.

It was found that the original "Metazene" (A) formulation was completely stable during the testing period employed and satisfactory in the clinical trials. Formulation B (quaternary) was found to be unsatisfactory due to a decrease in solubility of the quaternary caused by the addition of the type 12 propellant. Further studies showed that the percentage by weight of the absolute ethanol had to be increased to a minimum of 10 percent by weight to provide complete solubility for the quaternary.

It is concluded that the "Metazene" formulation provides simplicity of formulation, prompt and lasting effect, stability, nonflammability, and freedom from ordinary hazards of toxicity.[9,11,15] It is also concluded that the aerosol equipment used and the physical facilities utilized are well-suited to aerosol formulation. With several minor modifications and changes, primarily in the physical layout and fixtures, the aerosol formulation laboratory can also function as an aerosol production laboratory for general hospital use. The formulation and packaging of space deodorants were intended only to illustrate the feasibility and applicability of a small scale aerosol laboratory in a hospital pharmacy manufacturing program.

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The preparation and anti-bacterial action of TWEEN-20 IODINE

Preparations of formulations of Tween-20 Iodine

by EDWARD N. DEEB *and* JOHN W. BOENIGK

► THE VETERANS ADMINISTRATION HAS BEEN CONcerned with the problem of an effective disinfectant for thermometers for some time. A research project by Sommermeyer and Frobisher[1, 2] established the superiority of iodine for the disinfection of thermometers. The Veterans Administration adopted the results of their work and required the mandatory use of a 1 percent solution of iodine in 70 percent alcohol for the disinfection of thermometers in all Veterans Administration hospitals.

This iodine preparation has a number of disadvantages. Iodine is slowly soluble in 70 percent alcohol when no iodides are present, and a considerable length of time was required for complete solution of the iodine. The irritating odors of alcohol and iodine were especially noticeable during the preparation and use of this tincture. Large volumes of the tincture were required by the nursing stations, yet the pharmacy department hesitated to prepare large stocks of the preparation because it had to be stored in glass containers and if the containers were broken, the surrounding area would be stained and a possible fire hazard created.

An attempt was made by the pharmacy department in 1954 to prepare a concentrate which would overcome the disadvantages entailed in the preparation and use of the 1 percent tincture. Experimentation established the fact that iodine could be quickly solubilized by Tween 20* and Tween 80*, and that the concentrate could be readily diluted to a 1 percent tincture as well as an aqueous solution. The iodine is solubilized due to the formation of a complex of iodine and the surfactant (Tween 20). This type of complex is called an iodophor. Other problems took precedence over this project and further work was postponed.

The reported increase of staphylococcal infections in hospitals resulted in a re-evaluation of general purpose disinfectants. One of the results of this re-evaluation was the demonstrated value of iodophors. A number of iodophor formulations have been tested both in the laboratory and clinically and have received acceptance by a number of hospitals.

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Iodine has been valued as an effective germicide by a number of authors.[3-6] It has the special advantage of being a non-specific antibacterial as well as a virucidal and fungistatic agent. In most cases, iodine is effective within a very short period of time.[7] Because of its effectiveness, it has been recommended for a wide variety of uses.[3-5]

In spite of the antibacterial effectiveness of iodine, its use has been limited because of the objectionable physical and chemical properties of iodine and its previously available preparations.[8] Iodine has been used mostly in the form of aqueous or aqueous-alcoholic solutions. Aqueous solutions of iodine are antibacterial; however, iodine is only slightly soluble in water (33.5 mg. per 100 ml.). The saturated aqueous solution would retain its antibacterial effect for only a short time as the iodine would soon be bound with bacteria or other protein material. The solubility of iodine in water can be increased by the addition of alkali iodides; however, the iodine-iodide complex ties up much of the iodine and only the I_2 form has significant antibacterial activity.[9] Aqueous solutions of iodine and alkali iodides lack the penetration qualities of alcoholic solutions of iodine, they are less effective antibacterials and they are irritating due to their salt content.[10]

Iodine is soluble in 95 percent alcohol and other organic solvents; but, these solutions cannot be diluted with water without precipitation of the iodine. Alcoholic solutions of iodine containing an alkali iodide may be diluted with water without precipitating the iodine. Alcoholic solutions have the further disadvantage of causing additional irritation when applied to open wounds or cuts. Both aqueous and alcoholic solutions of iodine have the following disadvantages: they are corrosive, cause staining of clothing and skin, and they are irritating to skin tissue as well as to the nostril and eyes.

Aqueous solutions of iodophors have overcome most of the disadvantages of previous iodine preparations, yet they retain the bactericidal effectiveness of iodine. Because of the reported effectiveness of other iodophors,[3, 10] a decision was made to investigate completely the possibilities of Tween 20-iodine.

Objectives

The objectives of this research project were:

1. To prepare formulations of Tween 20-iodine.
2. To determine the stability of Tween 20-iodine complex and its preparations.
3. To test the antibacterial effectiveness of Tween 20-iodine.
4. To determine if Tween 20-iodine preparations cause irritation or produce sensitivity.

*Trademark of the Atlas Powder Company, Wilmington, Delaware, for its brands of polyoxyethylene sorbitans.

Table 1. Determination Of Available Iodine

Preparation	Assayed Available Iodine, %
PVP-Iodine Solution, 1%[a]	1.078
Lugol's Solution, 1%	0.996
Tween 20-Iodine Solutions, %[b]	
0.1	0.071
1.0	0.702
1.4	0.987
5.0	3.510
10.0	7.020

a. Contains 1 percent available iodine according to manufacturer's label.

b. Percent is total iodine content not the available iodine. Assays indicate that the average percent of available iodine in the Tween 20-iodine samples was 70 to 71 percent.

To determine accuracy of the assay method, PVP-iodine solution containing 1 percent available iodine and Lugol's solution diluted to 1 percent iodine concentration were assayed at the same time.

Experimental

1. Preparation

Preliminary assays of Tween 20-iodine established that only 70 percent of the total iodine used in preparation of the complex was released as available iodine upon dilution, hence a 30 percent excess of total iodine must be used to obtain the desired concentration of available iodine.

A Tween 20-iodine concentrate containing 10 percent available iodine may be prepared by either of the two following methods. This concentrate can be used to prepare tinctures, solutions or ointments of lesser concentrations of available iodine.

A. Trituration

Finely powdered iodine (14.25 Gm.) is placed in a glass mortar. The Tween 20 is weighed (85.75 Gm.) in a bottle in which the preparation is to be stored, and then added to the iodine in portions with trituration between each addition. Solubilization of the iodine occurred within a few minutes.

B. Heat

An alternate method involving heat may be used. The finely powdered iodine and the Tween 20 are placed in an Erlenmeyer flask, the flask stoppered and warmed in a water bath at 50° C. The iodine dissolved upon slight agitation.

C. Tincture

A tincture may be prepared by dilution of a weighed quantity of the Tween 20-iodine concentrate with 95 percent alcohol.

D. Ointment

An ointment may be prepared by incorporation of a weighed quantity of the Tween 20-iodine concentrate with either an anhydrous or hydrous base.

Tubercle bacillus culture

2. Assay Method

An appropriate weight or volume of the sample was transferred to a 125 ml. flask by washing with five 10-ml. portions of distilled water and the solution titrated with 0.1N sodium thiosulfate. Starch test solution was added near the end point. Each ml. of 0.1N sodium thiosulfate is equivalent to 12.69 mg. of available iodine.

3. Irritation and Sensitivity Tests

Three drops of a 0.1 percent and a 0.25 percent aqueous solution made from the Tween 20-iodine concentrate were instilled into the left eye of three rabbits, the right eye serving as the control. The drops were measured from the dropper of a one-half fluid ounce bottle. The drops were placed into the conjunctival sac of the animal, the lower lid raised and the eye massaged several times. The test was performed four times daily for a two week period.

A 1 percent aqueous solution of the Tween 20-iodine was applied with rubbing to the shaved abdominal area of three rabbits two times a day for one week. The painted area was not covered. A 1 percent aqueous solution of PVP-Iodine* and a 1 percent Lugol's solution were applied at the same time for comparison purposes.

*PVP-Iodine is the trademark product of Tailby-Nason Company, Inc., Dover, Delaware.

Table 2. Stability Of Tween 20-Iodine Preparations

Total I_2 Content in Preparation %	Storage at Room Temp. Months	Theoretical* Available I_2 %	Assayed Available I_2 %
10.0[a]	17	7.00	6.91
10.0	11	7.00	6.60
6.0	2	4.20	4.21
4.3[b]	5	3.01	2.48
3.4[b]	1[d]	2.38	1.68
1.7[c]	16	1.16	1.14
1.4	2[d]	0.98	1.04
1.4	11	0.98	0.99
1.0	11	0.70	0.69
1.0	2	0.70	0.70

*On the basis of 70 percent of the total iodine content of the preparation being available iodine, as presented in Table 1.

a. Prepared with the aid of heat (50° C.).

b. Tincture made from the 10 percent Tween 20-iodine concentrate. The addition of ethyl alcohol resulted in an additional loss of the available iodine.

c. Ointment made from the 10 percent Tween 20-iodine concentrate.

d. Days.

Tubercle bacillus x 1,000

Table 3. Bactericidal Efficiency Of Tween 20-Iodine Against Mycobacterium Tuberculosis

Dilutions used (Available I_2)	Parts per million Iodine (p.p.m.)	Results (a)	Results (b)
1-50,000	20	+	—
1-25,000	40	+	—
1-15,000	66	—	—
1-10,000	100	—	—
1-5,000	200	—	—
Control	0	+	+

+ Indicates growth in Petragnani medium (modified) after 8 weeks incubation.

— Indicates no growth in Petragnani medium (modified) after 8 weeks incubation.

(a). Dilutions to be tested were inoculated with 0.1 ml. of a suspension containing *five* 8-mm. loopfuls of TB culture diluted to 10 ml. with distilled water.

(b). Dilutions to be tested were inoculated with 0.1 ml. of a suspension containing *one* 8-mm. loopful of TB culture diluted to 10 ml. with distilled water.

Controls showed growth after 20 days incubation.

Table 4. Bactericidal Activity Of Tween 20-Iodine Against Pseudomonas Aeruginosa and Micrococcus Variant Aureus

Dilutions used (Available I_2)	Parts per million Iodine (p.p.m.)	Results (a)	Results (b)
1-50,000	20	—	—
1-25,000	40	—	—
1-20,000	50	—	—
1-13,300	75	—	—
1-10,000	100	—	—
1-5,000	200	—	—
Control	0	+	+

(a). *Pseudomonas aeruginosa*

(b). *Micrococcus pyogenes* variant *aureus*

— indicates no growth after transfer into BHI broth and incubation for 72 hours.

+ Indicates growth after transfer into BHI broth and incubation for 72 hours.

Dilutions to be tested were inoculated with 0.1 ml. of a 24 hour culture of the organism.

A limited number of human irritation studies were made by applying a 5 percent aqueous dilution of the Tween 20-iodine concentrate to an open wound. The same solution was painted on the under surface of the upper arm and a bandage applied to the area for several hours.

4. Microbiological Testing

The test organisms used were *Mycobacterium tuberculosis, Micrococcus pyogenes* var. *aureus,* and *Pseudomonas aeruginosa.* All organisms were pathogenic and were isolated from hospital patients. The organisms were identified by clinical laboratory personnel. The *M. tuberculosis* was isolated from positive sputum and cultured on Petragnani's medium. A five week old culture of *M. tuberculosis* was used in these tests.

A. Bactericidal Activity of Tween 20-iodine on *Mycobacterium tuberculosis.*

The testing procedure was a modification of that used by Lawrence *et al.*[6] The required number of 8-mm. loopfuls of a colony of *M. tuberculosis* were placed in a sterile 50 ml. flask containing sterile glass beads. Ten ml. of sterile distilled water was added and the flask shaken until a uniform suspension of the inoculum was obtained.

To sterile 30 ml. screw-cap test tubes were added 5 ml. of diluted Tween 20-iodine. One-tenth ml. of the culture suspension and 5 ml. of distilled water were added to each test tube. At the end of ten minutes, 1 ml. of sterile 0.05 M sodium thiosulfate was added to inactivate the germicidal effects of the iodine.

Five-tenths ml. of each test suspension and an equal quantity of the distilled water control were inoculated onto the surfaces of modified Petragnani medium slants. The tubes were incubated at 37° C for two months and the presence or absence of growth was recorded. The dilutions used and the results obtained are shown in Table 3.

B. Bactericidal Action of Tween 20-iodine Against *Micrococcus pyogenes* var. *aureus,* and *Pseudomonas aeruginosa.*

One-tenth ml. of a 24 hour broth culture of the test organisms grown in Brain Heart Infusion broth was added to 5 ml. portions of the diluted Tween 20-iodine and to 5 ml. of a sterile distilled water control.

At the end of a one minute contact period, 1 ml. of sterile 0.05 M sodium thiosulfate solution was added to each tube containing Tween 20-iodine to inactivate the iodine. One-half ml. portions of each test suspension including the control were transferred to tubes containing 5 ml. of sterile Brain Heart Infusion broth. The tubes were incubated for 72 hours, at which time the presence or absence of growth was noted. The results of this test are shown in Table 4.

This bacteriological test was repeated with the same organisms against Lugol's solution and PVP-Iodine in equivalent iodine concentration.

Discussion

1. Preparation

Two methods are given for the preparation of Tween 20-iodine containing 10 percent available iodine. It is possible to solubilize up to 32 percent total iodine in Tween 20; however, a 10 percent solution is more convenient to use. The percent concentration is expressed on a weight to weight basis because it is difficult to accurately measure Tween 20 by volume.

A 30 percent excess of total iodine is required since only 70 percent of the iodine added is available for titration or bactericidal action. The retention of a portion of the iodine in Tween 20-iodine as non-available or bound iodine is not unique as most iodophors bind various percentages of the total iodine added. The iodine is reportedly bound by the surfactant in molecular aggregates called micelles. The micelles are formed in the solution when a definite concentration of the surfactant has been exceeded.[7, 10]

Iodine may be solubilized by anionic, cationic and nonionic surfactants. No effort was made to investigate any surfactant other than Tween 20 in this research problem.

2. Irritation and Sensitivity Studies

A limited number of irritation and sensitivity tests were conducted on the eyes and shaved abdominal area of rabbits. The tests indicated that only slight irritation occurred which cleared up within 15 to 30 minutes. No evidence of primary irritation was observed when the 1 percent solution of Tween 20-iodine was applied to the shaved abdominal area of rabbits. No evidence of developed sensitivity was observed with either test.

Only a limited number of human irritation tests were made. The application of a 5 percent aqueous solution of the Tween 20-iodine concentrate caused only slight transient irritation. Application of the same solution to the inner aspect of the upper arm and the area bandaged for several hours caused no apparent irritation.

3. Microbiological Tests

Aqueous solutions of Tween 20-iodine were tested and found to be effective bactericides against *Mycobacterium tuberculosis, Micrococcus pyogenes* var. *aureus,* and *Pseudomonas aeruginosa.* Tween 20-iodine was found to be effective against gross contamination of *Mycobacterium tuberculosis* at a concentration of 70 parts per million (p.p.m.) of available iodine, and against a lesser contamination at a concentration of 20 p.p.m. of available iodine. Tween 20-iodine was also found to be effective against *Micrococcus pyogenes* var. *aureus,* and *Pseudomonas aeruginosa* at a concentration of 20 p.p.m. of available iodine.

Summary

1. Iodine is unique among the known bactericides and disinfectants in that it is equally effective against various bacteria, and is also effective against fungi and viruses. The use of iodine has been limited because of the disadvantages of previously used iodine preparations. Recently developed iodine complexes with surfactants (iodophors) have overcome most of the disadvantages of previous iodine preparations while retaining the bactericidal effectiveness of iodine.

2. Tween 20 will solubilize up to 32 percent (w/w) iodine, and form a stable iodophor. Two methods are described for the preparation of Tween 20-iodine concentrate containing 10 percent available iodine.

3. The Tween 20-iodine iodophor is soluble in alcohol, water or aqueous-alcoholic solutions.

4. Assays of Tween 20-iodine and its preparations show that 30 percent of the total iodine added is bound to the Tween 20 and is not available for titration or bactericidal action.

5. The Tween 20-iodine concentrate can be readily incorporated into both hydrous and anhydrous ointment bases. The ointment made with the anhydrous base was the most stable.

6. Irritation and sensitivity tests on the eyes and shaved abdominal area of rabbits indicated only slight transient irritation when a 0.1 percent and a 0.25 percent aqueous solution was instilled into the eyes of rabbits. A 5 percent solution applied directly to a wound caused no irritation. The same solution when painted on intact skin and the area bandaged for several hours caused no apparent irritation.

7. Aqueous solutions of Tween 20-iodine were tested and found effective at low concentrations against *Mycobacterium tuberculosis, Micrococcus pyogenes* var. *aureus* and *Pseudomonas aeruginosa.*

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MOBILE DISPENSING for the hospital pharmacy

by WILLIAM E. HASSAN, JR.

► ONE OF THE MOST COMMON ROUTINES PRACTICED by the hospital pharmacist, in both large and small institutions, is the stocking of the medicine cabinets on the nursing stations. This procedure is usually accomplished by the filling of the daily ward basket. There are, however, some institutions employing the mobile pharmacy technic whereby the drug basket is abandoned and the supplies are transported to the floor, by the pharmacy staff, in specially constructed trucks.

The purposes of this paper are to (1) document the advantages offered by the mobile pharmacy type of floor stocking, (2) outline some necessary phases of the program which must be considered prior to commencing such a procedure, (3) to present a brief description of a specially constructed truck which has demonstrated its adequacy over a five-year trial period, and (4) to describe briefly a *modus operandi* of a mobile dispensing unit.

Advantages of a Mobile Pharmacy

1. Drugs are, at all times, under the control of either the Pharmacy or Nursing Service. This obviates theft of, or the tampering with supplies by lay help.

2. It brings the pharmacist into direct contact with both the professional and nonprofessional staff.

3. All drug supplies on the nursing station are kept up to standard quantities by the pharmacy. Busy nurses often fail to check their inventory and often "run out" or are conversely over-stocked.

4. The decision as to whether the drug containers are uniform and clean is made by a pharmacy employee.

5. Out-dated or deteriorated drugs are immediately removed and replaced by experienced and trained personnel.

6. Non-floorstock items are quickly removed before they accumulate and get into use, thereby creating a potential revenue loss to the pharmacy.

7. The nursing station drug cabinet is continually checked by the pharmacist to prevent the mixing of internal use and external use medications in the same unit. (Prohibited by law in some states.)

8. The pharmacist is available for "on-the-spot" consultation by members of the nursing or medical staff.

9. The time of nursing, orderly, and housekeeping personnel is saved by the elimination of drug baskets.

10. The cost of drug delivery is, by this method, actually carried as a true pharmacy operating expense.

11. Because of the close supervision afforded the floor inventory by trained personnel, it is possible to restrict the stocking procedure to three mornings per week.

12. This method of floor stocking is more adaptable to a prepackaging operation.

Preliminary Preparation

Prior to initiating this type of service, the concept and advantages of such a system must be clearly explained to the members of the Pharmacy Committee and the Nursing Service. Our experience has demonstrated that the method is readily acceptable to the Nursing Service in view of the fact that they are relieved of the task of inventorying and ordering of routine floor stock.

An important step is to review, with the Pharmacy Committee, the present list of floor stock medications. The purpose of the review is to eliminate seldom used

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items, products of similar therapeutic efficacy, and duplicate emergency drugs which are normally stocked in a "stat" box or cart. By so condensing the floor stock inventory, it becomes adaptable to a prepackaging program and truck delivery procedures. A tabulation of the floor stock items and sizes of the containers, used in this Hospital is presented in Table I.

Truck Construction

The mobile pharmacy trucks used at the Brigham were especially constructed of stainless steel. Each unit measures 60″ high, 48″ wide, and 25½″ in depth. The main body is mounted on six balloon tires, 8″ in diameter. The center two wheels are stationary while the forward and rear ones are swivel-type. The right hand side of the body has two sliding doors equipped with a locking device. The top of the body has a two-inch rim which allows empty bottles to be carried there without sliding off. The base of the body is surrounded by a heavy duty steel and rubber bumper. (See illustration No. 1.)

The interior of the unit consists of four shelves so arranged as to allow for the storage of various sized containers ranging in size from ounce to one gallon. (See illustration No. 2.)

Obviously these trucks can be fabricated from other materials such as wood or aluminum or a combination of materials. Stainless steel was the choice for the above described units because of the ease with which it could be maintained; however, it was necessary to sacrifice some maneuverability due to the difference in weight.

Use of the Mobile Unit

Ideally, two mobile units are put into operation. This allows one unit to be in use while the other is being cleaned and restocked.

The delivery hours and days can be selected in cooperation with the Nursing Service. The period of choice would be when there exists the least amount of traffic on the pavilion. The early morning (7:00 A.M. - 8:00 A.M.) or the late afternoon (3:00 P.M. - 4:00 P.M.) periods are usually most acceptable. Days of delivery may be Monday, Wednesday and Friday, or Tuesday, Thursday and Saturday. No deliveries are scheduled for Sundays and holidays.

The pharmacist should be provided with a master key to the drug cabinets in order to allow him to service them without relying on the availability of the head nurse.

The pharmacist should, while at the drug cabinet, check off the desired items on the Ward Requisition Sheet. The carbon copy of this sheet is left on the pavilion as a record of the delivery, and the original is returned to the pharmacy where it will serve three purposes (1) to re-stock the mobile unit, (2) to determine rate of use of the various products for manufac-

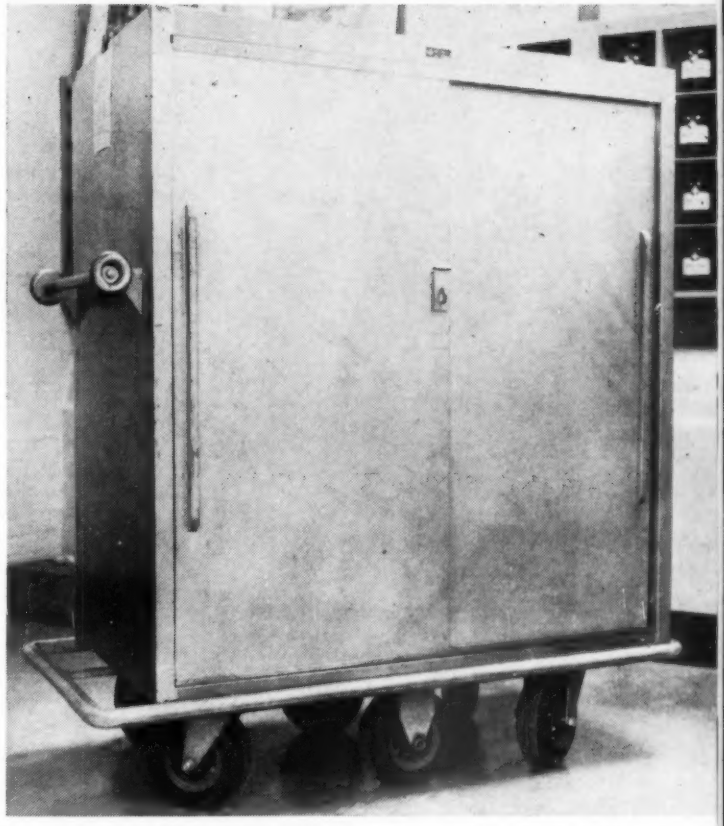

Fig. 1 View of drug cart showing closed doors, arrangement of casters, bumper and handle

Fig. 2 Drug cart open to show arrangement of containers and shelving of the unit

Table I. Drugs and Supplies With Sizes of Containers Supplied As Floor Stock at Peter Bent Brigham Hospital

AMPULS

Adrenalin 1 cc. 1:1000
Aminophylline 10 cc. 250 mg.
Atropine Sulfate 20 cc. 0.4 mg./cc.
Digitoxin 1 cc. 0.2 mg.

CAPSULES AND TABLETS

Acetylsalicylic Acid 0.3 Gm.
Acetylsal. Acid Comp.
Ammonium Chloride E. C. 0.5 Gm.
Atropine Sulfate TT 0.65 mg.
Cascara Sagrada Extract 0.3 Gm.
Iopanoic Acid (Pkges of 6)
Nitroglycerin H. T._____mg.
Placebos (Blanks)
Potassium Chloride E.C. 0.3 Gm.
Quinidine Sulfate 0.2 Gm.
Sodium Bicarbonate 0.6 Gm.
Sodium Chloride E.C. 1.0 Gm.

OINTMENTS AND CREAMS

A & D Ointment, (4 oz.)
Lanolin, (4 oz.)
Lanolin-Stearin Cream, (4 oz.)
Petrolatum Amber, (4 oz.)
Zinc Oxide & Castor Oil Oint., (4 oz.)
Zinc Oxide Ointment, (4 oz.)

POWDERS

Dextrose (100 Gm. units)
Sodium Bicarbonate, (16 oz.)
Talcum, (16 oz.)
Thymol Iodide, (2 oz.)

REAGENTS

Acetone, (8 oz.)
Acetic Acid_____%, (4 oz.)
Ammonia_____10% or_____28%, (4 oz.)
Benzidine Reagent, (4 oz.)
Guaiac-Tincture, (2 oz.)
Hydrochloric Acid_____%, (4 oz.)
Schiller's Solution, (8 oz.)
Sulfuric Acid 50%, (2 oz.)
Toluene, (8 oz.)
Topfer's Reagent, (4 oz.)
Wright's Stain, (8 oz.)

SOLUTIONS

Alcoholic Sponge Lotion, (32 oz.)
Alkaline Aromatic Solution, (32 oz.)
Aromatic Spirit Ammonia, (2 oz.)
Back Rub Lotion, (32 oz.)
Belladonna Tincture, (4 oz.)
Benzalkonium Chloride 1:750
(for Skin Disinfection), (32 oz.)
Benzalkonium Chloride 1:1000, (128 oz.)
Benzalkonium Chloride 1:20,000, (128 oz.)
Benzalkonium Chloride Tincture, (16 oz.)
Benzoin Tincture, (4 oz.)
Benzoin Compound Tincture, (4 oz.)
Calamine Lotion, (8 oz.)
Cascara Fluid Extract Aromatic, (4 oz.)
Castor Oil, (8 oz.)
Chloral Hydrate 1 Gm./5 cc., (8 oz.)
Chlorinated Soda 5%, (32 oz.)
Collodion Flexible, (4 oz.)
Cottonseed Oil, (8 oz.)
Denatured Alcohol for Lamps, (8 oz.)
Deodorizing Spray, (16 oz.)
Ether Not for Anesthesia, (8 oz.)
Ether-Alcohol Mixture, (8 oz.)
Glycerin, (8 oz.)
Hand Lotion, (8 oz.)
Hexachlorophene Soap, (32 oz.)
Hydriodic Acid Syrup, (4 oz.)
Hydrogen Peroxide 3%, (16 oz.)
Iodine Aqueous 2%, (8 oz.)
Iodine PVP Concentrate, (8 oz.)
Iodine Tincture 2%, (8 oz.)
Instrument Sterilizing Solution
(Zephicide), (32 oz.)
Isopropyl Alcohol 50%, (32 oz.)
Magnesia Magma (Milk of Magnesia), (32 oz.)
Mag. Sulfate & Glycerin eq. pts., (16 oz.)
Opium Camphorated Tr. (Paregoric), (2 oz.)
P. C. G. Solution, (8 oz.)
Peppermint Spirit, (2 oz.)
Petrolatum Liquid (Mineral Oil), (32 oz.)
Phenylephrine HCl. Nasal ¼%, (2 oz.)
Potassium Permanganate 1:_____, (32 oz.)
Sodium Hypochlorite 1:1000, (16 oz.)
Terpin Hydrate Elixir, (4 oz.)
Terpin Hydrate Elixir with Codeine, (8 oz.)
Thermometer Germicide Solution, (32 oz.)
Vanilla, Compound Tincture, (32 oz.)

turing and purchasing programs, and (3) to serve as the charge slip for the allocation of drug costs to the individual pavilions.

Upon the return of the mobile unit to the pharmacy, the re-stocking procedure need not be immediately commenced. This can be reserved until later in the day or even the next day when student pharmacists (who can be easily trained to perform this task) on the staff may be available. Obviously, all labeling and re-filling procedures carried out by the student pharmacist must be under the supervision of a staff pharmacist. As an added precautionary measure all ward stock containers, filled from bulk storage, should carry an auxiliary label showing the lot number of the product.

Economics of a Mobile Pharmacy

Prior to initiating the mobile pharmacy program, the cost of delivering ward stock to the floors was calculated to be approximately $93.00 per week.

This figure was arrived at as follows:

1. Night orderly to pick up ward baskets and deliver them to the pharmacy (1 hour)	$ 1.25
2. Day orderly to return filled baskets to the pavilions (1 hour)	$ 1.25
3. Two pharmacists to fill containers etc. (1 hour)	$ 6.00
4. Pharmacy student to re-stock unit	$ 2.00
5. Nursing time devoted to trips to Pharmacy for stock which ran out, was not delivered, etc.	$ 5.00
	$15.50 per day.

$15.50 x 6 days = $93.00 per week.

With the mobile pharmacy unit in operation, the cost of delivering ward stock to the pavilions was reduced by nearly 50 percent as follows:

1. One (1) pharmacist to operate truck 1½ hours	$4.50
2. Pharmacy student to re-stock unit	$2.00
3. Nursing time now devoted to pickups	$2.50
	$9.00 per day.

$9.00 x 6 delivery days* = $54.00.

*If delivery can be reduced to every other day the cost would also drop proportionately.

Conclusion

A mobile pharmacy service can be initiated in any hospital at a minimal cost. No additional personnel is required and maximal safety, legal, and inventory controls are acquired. Futhermore, a reduction in the delivery cost of pharmaceuticals to the pavilions is realized.

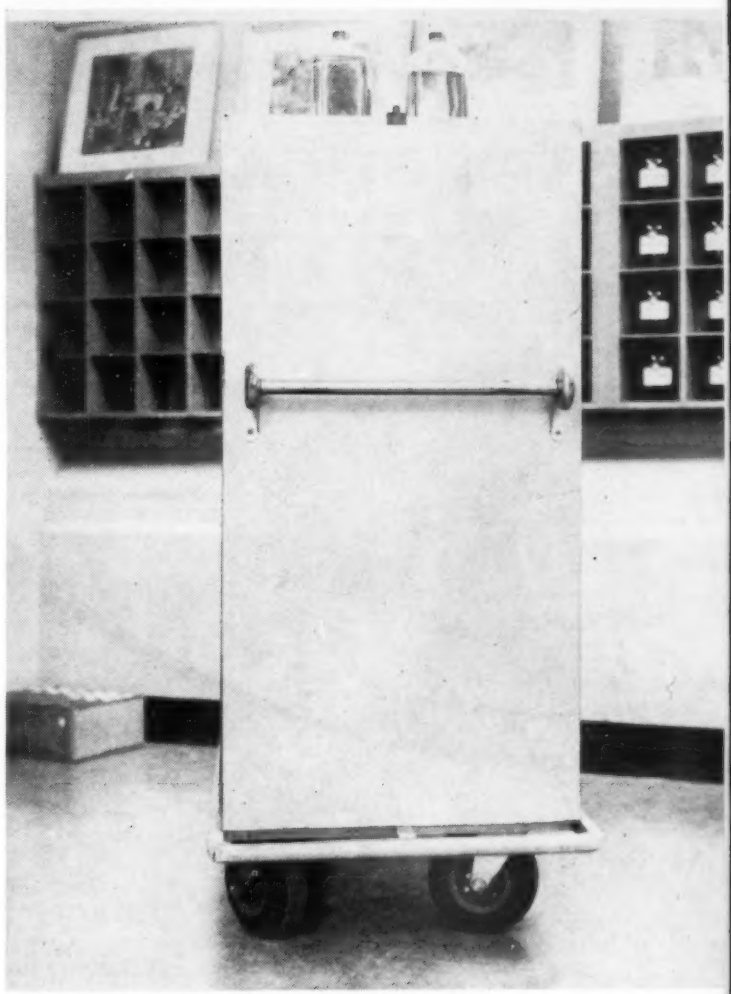

Fig. 3 End view of the drug cart shows two inch rim on top of truck to hold empty return containers from the pavilions

VALUE OF STATISTICAL REPORTING OF POISONINGS

FROM DRUGS & HOUSEHOLD PRODUCTS

by HENRY L. VERHULST

► AT ITS INCEPTION, IT WAS RECOGNIZED that a poison control center reporting system could be the source for epidemiologic data concerning poisoning and could be valuable in the collection of data relating to toxicity in human beings of new household products and drugs. The data presented here illustrate what information concerning human toxicity experience can be derived from such a reporting system.

Reporting Forms

A standard report form is used to record cases treated by local centers and each telephone inquiry answered by the centers. The form was designed to provide the following information: description and amounts of substance ingested, clinical and laboratory findings; treatment given or recommended; length of hospitalization; identifying facts about the victim (name, age, and sex). In some cases, further information concerning storage of the toxic or potentially toxic substance, supervision of the victim at the time of the accident, and other circumstances surrounding the accident, was obtained from a home visit usually made by a public health nurse.

One can realize how important it is that poison report forms are filled out as completely as possible. It follows that pertinent information is lost when the forms are incompletely filled out.

There are 14,069 cases of accidental ingestion reported to the National Clearinghouse by 60 centers for various time periods from 1954 to 1958. Of this number 10,129 were reported in 1958. Tabulations by broad breakdown for 1958 show medicines (external 724, internal 4,003) accounted for 4,727 or 46.7 percent, household products 1694 or 16.8 percent, petroleum products 507 or 5 percent, pesticides 1026 or 10.1 percent, and cosmetics 496 or 4.9 percent. These were followed by paints and varnishes, and plants. Plants accounted for 275 or 2.7 percent of the ingestions.

As has been reported so often before, aspirin accounted for approximately 50 percent of the medications ingested. This was followed by barbiturates, laxatives, tranquilizers, cough medicines, and antihistamines. Anti-infectives which are generally reported as one of the top prescription groups (1) accounted for only 1.4 percent of the total ingestions.

There were 30 deaths reported for the total 14,069 poisoning accidents—a case fatality rate of 2.1 per 1,000 accidental ingestions. Eighteen of these deaths occurred in children under 5 years of age (case fatality rate - 1.5) One-year old children accounted for 10 deaths (case fatality rate - 2.6).

Medicines caused 8 deaths, 5 in children younger than 5 years. Petroleum products were involved in 8 deaths, 7 occurring in children younger than 5 years. Six deaths were caused by ingestion of pesticides, 4 occurring in children younger than 5 years. The case fatality rates for children younger than 5 years for specific substances are as follows: medicines 0.9, petroleum products 10, and pesticides 3.4.

Approximately 90 percent of the ingestions occurred in children under 5 years of age. Approximately two-thirds of the children were between the ages of 12 and 36 months.

The foregoing figures may seem small to you. However, remember that it is estimated that 600,000 ingestions occur each year. There are approximately 1400 deaths from ingestion of liquids and solids, 450 of which are among children under 5 years of age.

Types of Products Ingested

As a pharmacist, I believe that several important facts have been shown in this study. Analysis of the type of product ingested by the age of the child in years shows that the one-year old has a greater tendency to ingest cleaning and polishing agents, pesticides, and petroleum distillates along with medications; however, as he grows older, there is a shift in type of substance ingested to medications. In the three year age group,

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Presented at the Pharmacy Section, American Association for the Advancement of Science, December 29, 1959, Chicago, Illinois.

1. *American Druggist*, September 21, 1959.

60 percent of the reported ingestions are medications. This is 59 percent at 4 years. There are less ingestions in these older age groups. Further research is necessary to determine what role the child's observation of the parent taking medicine and his desire to mimick the parent may play in this problem.

The item ingested was found most frequently in the kitchen, then the bedroom, bath, living room, and garage, in that order. Of particular interest to us have been the reports that the items ingested are not in their customary places of storage. For example, when we survey those items which were reported as having been ingested in the kitchen, we find that 64 percent were not in their customary place of storage and 29 percent were not in the original containers. One of our problems in education and prevention is to get the parents to return household products to a safe place after using them.

Petroleum Distillates

I would like to devote several minutes to discuss the types of projects which can be carried out through mass reporting. Petroleum distillates have for some years accounted for a significant percentage of the deaths from accidental ingestion of toxic substances in the age group 5 years and under. Death is generally the result of pneumonitis or pulmonary edema which results primarily from the aspiration of some of the material. Some authorities have held, however, that even when aspiration does not occur, the hydrocarbon may be absorbed from the gastrointestinal tract and carried to the lungs where it infiltrates and irritates the tissue.

Most authorities agree that vomiting should not be induced following the ingestion of petroleum distillates. However, there are two schools of thought concerning lavage. One group feels that lavage should not be performed while the other group, believing that absorption takes place, favors cautious lavage.

In 1957 a research project was planned by the American Public Health Association and the Public Health Service to evaluate the value of lavage versus no lavage. Hospitals in various sections of the country were asked to report all cases of kerosene ingestion to the National Clearinghouse on a special form following a plan for alternating lavage and no lavage. As of May 15, 1959, 45 hospitals had reported 631 cases. The present trend suggests that the preferred treatment is that of lavage, and that more complications occur if vomiting is induced than in cases in which the stomach is not emptied.

I would like to interject a note of caution here. In some instances the petroleum distillate may be the vehicle for a substance which is highly toxic. In such an instance the physician must consider the need to take a calculated risk at times and recommend vomiting.

Tranquilizers

Tranquilizers have made a tremendous impact on the pharmaceutical industry in the past few years. An infinite number of articles have been written on use and misuse of these drugs. A review of all accidental ingestions of tranquilizers was undertaken to determine how many cases we had and what the manifestations were.

In the four year period 1954 - 1958 (ending December 31, 1958), 280 cases of ingestion of and poisoning from psychopharmacologic agents were reported. These represent an incidence of 2 percent of all cases reported. Children under five years of age accounted for 163 or 58.2 percent of the 280 cases of tranquilizer ingestion. Thirty percent (84 cases) of ingestion of psychopharmacologic agents involved adults.

Phenothiazine derivatives were reported to be ingested in 89 instances. Children 4 years of age and younger accounted for 51 of these cases, while adults were involved in 28 of these cases. Manifestations following ingestion were reported for 38 cases (42.7 percent). These occurred in 20 of the 28 cases involving adults and 17 of the 51 cases involving children 4 years of age and younger.

Thirty-nine cases of chlorpromazine ingestion were reported. Twenty-six of these cases occurred in children 4 years of age and younger, 8 in adults. Manifestations were reported to occur in 14 instances following ingestion. Mild central nervous system depression was the most frequent manifestation recorded. Coma, miosis, hypotension, and respiratory arrest were also seen with this drug. Mild central nervous system depression was the most frequent manifestation following ingestion of prochlorperazine, perphenazine, and promazine.

Prochlorperazine was ingested in 19 instances; 8 ingestions were followed by manifestations. We learned of five oculogyric crises in a 4-month old infant who was given seven 2.5 mg. rectal suppositories of prochlorperazine over a period of three days; this dosage is probably too high for a child of this age. Marked twitching of the upper extremities, neck, and head were reported to occur in a 70 year old man following ingestion of 13 doses of 10 mg. of prochlorperazine over an unreported period of time, and "convulsions" were reported to have occurred in a 17 year old boy who received 16 doses of 10 mg. of the drug over a 4-day period; 40 mg. per day for adults is not considered an unusually large amount.

Reserpine and other rauwolfia derivatives were reported to be ingested in 79 instances, children 4 years and younger being involved in 73 of these. Manifestations were reported following approximately one-third

of the ingestions involving reserpine. Mild central nervous system depression and flushing of various parts of of the body were the manifestations most frequently noted. Restlessness, vomiting, miosis, hypotension, and muscular twitching also were reported. No serious nervous system manifestations such as coma or convulsions were reported.

Meprobamate was ingested in 93 instances. Children under 4 years of age accounted for 26 of these ingestions (28 percent) and adults over 20 years of age accounted for 52 of these cases (55 percent). Manifestations of overdosage followed ingestion in 47 instances (61 percent). These manifestations occurred in 44 of the 52 adult cases, and in only 5 of the children under 4 years of age who accidentally ingested meprobamate. Mild central nervous system depression was reported most frequently following single overdosage. In adults, serious central nervous system manifestations—coma, convulsions, ataxia, and hypotension—were reported to occur following ingestion of meprobamate in 19 instances.

Treatment

Emptying of the stomach was performed as soon as possible in many cases reported here, even after manifestations of overdosage were evident. Symptomatic and supportive treatment directed toward central nervous system depression and hypotension included administration of intravenous fluids and electrolytes, vasopressors, and oxygen and artificial respiration where indicated. Central nervous system stimulants were used in 24 cases manifesting varying degrees of depression. Caffeine sodium benzoate was used most frequently, usually for mild central nervous system depression. Methylphenidate was used next most frequently in treatment of cases of mild depression and of coma. Amphetamine, nikethamide, and pentylenetetrazol also were used, the last named being used in a comatose adult.

The amounts of tranquilizer agents ingested were taken from those cases in which the stomach was not emptied or in which stomach emptying was delayed 1 hour or more after ingestion, except in those cases of serious central nervous system depression.

Data presented here cannot evaluate the use of central nervous system stimulants in cases of central nervous system depression resulting from overdosage with psychopharmacologic agents.

Camphor

Camphor and camphor preparations have been used for many years. In 1919 the *Journal of The American Hospital Medical Association* published an article on poisoning from camphor preparations. The picture has apparently changed little. In the relatively short span of our activity, we have received 33 reports of ingestion of camphor preparations in which toxic manifestations occurred. These preparations consisted mainly of camphorated oil, although a common liniment and a common chest rub are included. Twenty-one of the cases were in children 5 years and younger. Convulsions were reported in 13 (40 percent) of the cases with the patient being 5 years or younger in 10 cases. A 2 year old convulsed following ingestion of only 1 teaspoonful of camphorated oil. Additional symptoms reported are vomiting, confusion, mania, flushing, drowsiness, cyanosis, coma, and abdominal pain. Fortunately, there were no deaths among this group.

Iron

A study of the reports of the ingestion of iron preparations was done. Nineteen of 52 cases reported toxic manifestations, 2 terminating with death. Since January 1, 1959 we have had 1 additional death reported from this substance.

Conley[2] has recently brought the dangers of iron poisoning to the attention of the physician, and our findings again emphasize the need for immediate treatment of iron overdosage. Although the exact mechanism of iron intoxication is poorly understood, the stomach should be emptied by gastric lavage or emesis. The administration of edathamil calcium-disodium to increase the rate of excretion has been reported. Respiration should be supported. Supportive treatment for shock and dehydration should be instituted. Exchange transfusions have been used with some success in children whose condition has continued to deteriorate in the face of good supportive care. One of the cases reported was successfully treated with exchange transfusions.

Detergent Enemas

The material presented here has dealt mainly with drug ingestions, since most of you are allied with the medical field. Similar data can be derived on insecticides, cleaning and polishing agents, and other materials. Here are two incidents which might interest you. Many of you are familiar with the practice of using soap enemas. Some of your hospitals may still use them. We have 2 reports of women who decided they needed enemas. One selected a highly advertised liquid cleaning preparation which unfortunately contains kerosene and pine oil. She obtained violent results. The other used a liquid detergent preparation with little or no dilution. She got results also. Both were treated at poison control centers. If your hospital is using soap enemas, it would be advisable to stay with soap or with a preparation which has been tested for this purpose.

Parathion

Most of these accidents occur with the child gaining

access to a product and ingesting the contents or feeding it to a sibling. I have taken a few case reports to demonstrate that this is not always so. A small amount of the insecticide, parathion, was spilled on the porch by a parent. Her one year old child got it onto his body. Apparently the parents were not aware that this product is quite deadly by percutaneous absorption. Result: the child was dead on arrival at the hospital. Most of the organic phosphate cholinesterase inhibitors have some degree of toxicity by skin absorption. If these products are spilled on the skin or clothing, the clothing should be removed and the area washed thoroughly with soap and water. Rubber gloves should be used.

Zinc Stearate

For many years the manufacturers have cooperated with Food and Drug Administration and placed zinc stearate in sifter top cans to reduce the danger of inhalation. Recently, parents of a 1 year old child went into a pharmacy to purchase zinc stearate. The pharmacist did not have a commercial package. He did, however, have bulk zinc stearate which he dispensed in a wide mouth jar. While the child's diaper was being changed he picked up the open bottle and dashed the powder into his mouth and nose. Respiratory distress from inhalation occurred immediately. Treatment included oxygen, positive pressure rescusitation, bronchodilators, antibiotics, hydrocortisone, and parenteral fluids during 11 days hospitalization.

Camphor Preparations

Earlier I mentioned data on the ingestion of camphor preparations. Let us take a look at how 3 ingestions happened. (1) A child had a cold and mother decided to give him a dose of castor oil. She made the mistake of giving camphorated oil. (2) The second patient was 14 years old. He was sent to the store for castor oil. He waited on himself and picked up camphorated oil instead of castor oil. Upon his return his mother gave him the preparation without reading the label. (3) Patient number 3 was 70 years old. Again, she thought she was taking castor oil but picked up the camphorated oil bottle. Two of these patients were hospitalized although none were fatalities.

Methyl Salicylate

Members of the lay public are not the only ones careless with medications, unfortunately. Recently we had a report of a nurse accidentally ingesting methyl salicylate. Why? Another nurse on the ward had a stiff neck. She poured some methyl salicylate into a drinking container so an attendant could massage her neck. When this was finished, the container, still containing some methyl salicylate, was placed on the bookcase. The nurse entered the nursing station, filled the container with orange juice, and drank it. Many poisonings occur because toxic substances are placed in food containers.

Aspirin

With the many newspaper reports of the dangers from aspirin poisoning, you may be asked frequently what amount of aspirin can be fatal. It may interest you to know that we have a record of a death from 15 grains of aspirin given a 4 month old sick infant within 2 days (2 five grain doses 1 day and five grains the next). Sick infants are very susceptible to aspirin intoxication.

Preventive Measures

It is quite plain, I think, that there is a tremendous need for parent education if there is to be a reduction in the number of accidental ingestions by children. They must be made aware of certain safety measures. Medicines should be kept out of the reach of children. Non-edible substances should never be placed in food containers. Labels should be read thoroughly before any medication is given. When old medications or products are discarded, they should be flushed down the drain instead of placed in garbage receptacles where children may find them. Above all, an individual should call a physician immediately—not a day later—when he discovers that a child has ingested a questionable item.

One of the iron deaths points up this situation, which occurs too frequently. The child was not brought to a physician until 2 days after the ingestion. At that time his condition was critical.

Local pharmaceutical associations are in an excellent position to furnish speakers to local parents' groups to discuss this need for prevention. No one is better qualified than you are to discuss precautionary measures. Certainly your background and training has given you a prestige in the community which will enable you to convince parents that medications, insecticides, lye, cleaning solutions, and the many other products which are found in the house should be kept out of the reach of young children.

Some accidents will continue to happen. Treatment will be necessary in these cases. Have you joined with the medical staff of your hospital to see that proper medications and equipment are in the emergency room to treat poisonings? Is your staff familiar with the large amounts of material you have in your pharmacy library which may be of value in treating drug overdose?[2] I find the *U. S. Dispensatory* and several of my pharmacy texts to be of great value when seeking information on toxicity. If you have not taken part in these activities, you should start now.

2. *J.A.M.A.* 170:676 (June 6, 1959)

Therapeutic Trends

edited by WILLIAM JOHNSON

Homochlorcyclizine—An Antiallergic

Homochlorcyclizine (N - p - chlorobenzhydryl - N′ - methyl-homopiperazine dihydrochloride) has been shown to possess a wide range of clinical effectiveness by Fisherman *et al.* as reported in *J. Allergy 31*:232 (May-June) 1960. A valuable adjunct in the symptomatic treatment of a number of allergic manifestations, it replaces neither antihistamines, bronchodilators, sympathomimetics, nor anti-inflammatory drugs. It has some actions not obtainable with any of the above. It was found to be useful in certain types of asthma and allergic cough and resistant cases of seasonal and perennial allergic rhinitis, urticaria, dermatitis, and some other allergic and allergic-like manifestations. Homochlorcylizine was supplied by Abbott Laboratories, North Chicago, Ill.

KENNETH W. HUCKENDUBLER

G-27202 (Metabolite 1 Of Phenylbutazone)

Three hundred and fifty-three patients suffering from various rheumatic disorders were treated with G-27202, metabolite 1 of phenylbutazone. W. Graham in *J. Canad. Med. Assoc. 82*:1005 (May 14) 1960 reports that the response was excellent in ankylosing spondylitis and gouty arthritis. In osteoarthritis, rheumatoid arthritis and tendinitis, as well as in other miscellaneous rheumatic disorders, the drug may be worthwhile, but should be discontinued if there is no relief in 7-10 days. The majority of the complications were minor and transient in nature, and all major reactions subsided promptly on cessation of therapy. The danger of toxicity is reduced by close clinical observation and prompt withdrawal of the drug at the first sign of toxic reaction. Particular care must be observed in patients with a history of peptic ulcer, drug hypersensitivity and cardiac disease. Metabolite 1 (G-27202) is definitely less irritating to the gastrointestinal tract than the parent drug, phenylbutazone. The therapeutic effectiveness of G-27202 is perhaps a little less than that of phenylbutazone, but some patients who fail to respond to phenylbutazone may respond to G-27202 and vice versa. Two hundred and fifty complete blood studies carried out at intervals throughout the treatment period revealed no evidence of a toxic effect on the blood or bone marrow. Geigy Pharmaceuticals supplied G-27202.

SYLVIA SCHMIDT

Diloxanide In The Treatment of Amoebiasis

The percentage of cure of intestinal amoebiasis with diloxanide was 71 percent at the end of treatment, comparing favorably with the older amoebicidal drugs. While from the limited observation, only 33 percent of the cases remain cyst-negative at the end of two weeks, Mehta *et al.* report in *Trop. Med. Hyg. 63*:93 (Apr.) 1960, that they are of the opinion that it is a useful and safe amoebicide and merits further trials. The drug has no action on hepatic amoebiasis. No toxic side effects were noticed. Diloxanide was supplied as "Entamide" by Boots Pure Drug Co. (India) Private Limited.

KENNETH W. HUCKENDUBLER

A New Antitussive

The relative antitussive efficacy of alpha (dimethylaminoethyl) - ortho - chlorobenzhydrol hydrochloride (SL-501, Bayer B-186), codeine, dihydrocodeinone and several currently used non-narcotic antitussives has been appraised by a method in which experimental cough was induced by aerosolized N sulfuric acid in unanesthetized dogs. SL-501, a new non-narcotic antitussive, shows a potent and long-acting cough-suppressing activity in dogs. It has a relatively slower onset of maximum action than the narcotic drugs. SL-501 exhibits moderate local anesthetic effects and mild antispasmodic action. J. Chen *et al.* in *J. Pharmacol. Exp. Therap. 128*:384 (Apr.) 1960 state that it also causes some prolongation of sleeping time in pentobarbitalized

mice. No analgesic, sedative-hypnotic, antihistaminic or antiemetic properties were demonstrated. Acute and chronic toxicity studies in animals indicate that SL-501 is relatively nontoxic, and has a high therapeutic ratio. Current clinical trials in approximately 1,400 patients indicate that the drug also exerts an antitussive action in man. SL-501 was supplied by Schenlabs Pharmaceuticals.

SYLVIA SCHMIDT

Propanediol Dicarbamate—W-583

The report of this double blind, double dose study by Bodi *et al.*, appears in the *Am. J. Med. Sci. 239*:207 (Feb.) 1960. W-583 is 2-methyl-2-sec-butyl-1,3 propanediol dicarbamate. This product was found to be nontoxic, except for minimal respiratory depression, in animals. This property was not found to effect humans. The study showed that the onset of hypnotic effect was from one to six hours. The delay was attributed to varying rates of absorption. There were no reported cases of early morning hangover after 200 mg. and 400 mg. doses. The drug was shown to possess sedative and hypnotic characteristics and may find possible use for restless patients who are in danger of developing barbiturate addiction. Blood counts, urinalyses, and liver function tests remained normal throughout the study. Further clinical evaluation of the sedative and hypnotic properties of this drug is recommended by these investigators. W-583 was supplied by Wallace Laboratories.

DALE R. HYDER

Treatment Of Corneal Abrasion With Topical Whole Blood

In addition to the usual treatment of corneal abrasion, i.e., application of antibiotic solution, homatropine for miotic spasm, and tight bandage, Christenberry reports in *A.M.A. Arch. Ophthalmol. 63*:948 (June) 1960, the instillation of whole blood into the conjunctival sac before the bandage is applied. This is done by squeezing a few drops of blood from the patient's finger directly into the eye. The bandage is left on for 24 hours. The treatment is repeated if necessary. No anesthetic medication is prescribed.

KENNETH W. HUCKENDUBLER

Valmethamide—Anxiety-Reducing Drug

Valmethamide, a new tranquilizer, has been studied for more than one year in a total of 97 patients ranging in age from 9-72 years. W. Stepansky in *Current Therapeutic Research 2*:144 (May) 1960 reports that the usual dosage was 200 to 400 mg. three or four times daily for periods varying from a few days to several months. The beneficial effect of valmethamide was noted by the patient within a short time after administration and was associated with infrequent and mild adverse effects. Valmethamide, a simple aliphatic acid amide, was found to be an effective tranquilizer in a general practice office for patients with anxiety-tension states resulting from acute environmental stress or from uncontrolled recurring internal conflict. Valmethamide was supplied as Axiquel by McNeil Laboratories.

SYLVIA SCHMIDT

Preliminary Evaluation Of Ro 2-5803

Green *et al.* tested a potential antiarrhythmic drug, 2,6,bis(1-piperidylmethyl)-4-(a,a-dimethylbenzyl) phenol dihydrobromide (Ro 2-5803). The drug was evaluated using mice, rats, and dogs as test animals. The drug was also tested on humans with and without heart disease, with sinus rhythm, atrial fibrillation and atrial flutter. In the test, reported in *Am. J. Cardiol 5*:806 (June) 1960, the drug was given to 23 patients intravenously, a total of forty-five times. The drug showed no untoward side effects at the dosage level, which began at 1 mg. and was increased to 150 mg. When atrial activity could be measured in the group with fibrillation, definite atrial slowing was in evidence. The drug demonstrated antiarrhythmic potential. The results also suggest that Ro 2-5803 may be of value in reversing adverse rhythm effects due to digitalis. There were no significant changes in blood pressure levels. This lack of hypotensive tendency after intravenous administration, if sustained at higher dose levels, would offer a desirable contrast to the hypotensive action of quinidine and procainamide.

RICHARD H. HARRISON

PA 155A—A New Antibiotic

A microorganism isolated from an African soil sample was designated as PA-3972 by the authors. This sample was found to be a strong antagonist to *Staphylococcus aureus* 376, a laboratory strain highly resistant to the tetracyclines, streptomycin, penicillin, and polymyxin. The microorganism was classified as a strain of *Streptomyces albus*. One of the active components of the microorganism was designated PA 155A. The production of the PA 155 antibiotics is dependent on the nature of the fermentation substrate employed. This screening for new antibiotics was done by Marsh *et al.* The findings were reported in *Antibiot. Chemotherap. 10*:316 (May) 1960.

RICHARD H. HARRISON

Timely Drugs

Astrafer I.V.

COMPOSITION: A soluble, high molecular, iron carbohydrate complex.

INDICATIONS: In anemias and iron deficiency; useful in late pregnancy, for replenishment of large iron deficits due to massive or repeated hemorrhage, or wherever rapid accumulation of iron is needed.

SIDE EFFECTS AND CONTRAINDICATIONS: Contraindicated in pernicious anemia, chronic leukemia, or bone marrow depression and liver damage.

DOSAGE: Initially, 1.5 ml. daily to be increased by daily increments of 1 to 1.5 ml. until a daily level of 5 ml. is reached. Discontinue treatment as soon as hemoglobin levels have been restored to normal. To be injected intravenously at a slow rate (not more than 5 ml. in 2 minutes).

PREPARATIONS: Iron carbohydrate complex equivalent to 20 mg. trivalent iron per ml.

PACKAGING: Ampuls containing 5 ml.; boxes of 10 ampuls.

SUPPLIER: Astra Pharmaceutical Products.

Cogentin Injection

GENERIC AND CHEMICAL NAMES: Benztropine methanesulfonate; tropine benzohydryl ether methanesulfonate.

INDICATIONS: Extrapyramidal reactions due to phenothiazine derivatives or Rauwolfia compounds; arteriosclerotic, idiopathic or postencephalitic parkinsonism.

SIDE EFFECTS AND CONTRAINDICATIONS: Has both anticholinergic and antihistaminic properties, and may produce side effects characteristic of either class of drugs.

DOSAGE: Must be individualized. Administered intramuscularly or intravenously. In parkinsonism induced by phenothiazines or Rauwolfia compounds, dosage is 1 to 4 mg. once or twice daily. In arteriosclerotic, idiopathic or postencephalitic parkinsonism, 1 to 2 mg. daily, with a range of 0.5 to 6 mg. daily.

PREPARATIONS: Ampuls containing 2 mg. benztropine methanesulfonate per 2 ml. (1 mg. per ml.).

PACKAGING: Boxes of 6 ampuls, 2 ml. each.

SUPPLIER: Merck Sharp & Dohme.

Ismelin

GENERIC AND CHEMICAL NAMES: Guanethidine sulfate; [2-(octahydro-1-azocinyl)-ethyl]-guanidine sulfate.

INDICATIONS: Treatment of almost all forms of moderate to severe hypertension.

SIDE EFFECTS AND CONTRAINDICATIONS: Should be used with caution in patients with severe coronary insufficiency or recent myocardial infarction; should be used cautiously in hypertension associated with renal disease with nitrogen retention, cerebral complications, or encephalopathy. Contraindicated in patients with pheochromocytoma; weight gain or occurrence of frank edema should be watched for.

DOSAGE: Individualization of dosage is essential; treatment should begin with small doses (10 mg.) which should be increased gradually. Has a long duration of action; therefore, increases should be made no more often than every 5 to 7 days unless patient is hospitalized.

PREPARATIONS: Tablets containing 10 mg. and 25 mg. guanethidine sulfate.

PACKAGING: Bottles of 100 tablets.

SUPPLIER: Ciba Pharmaceutical Products.

Lucanthone

CHEMICAL NAME: Lucanthone hydrochloride, a non-metallic thioxanthone derivative.

INDICATIONS: Oral treatment of schistosomiasis.

SIDE EFFECTS AND CONTRAINDICATIONS: Occasionally, anorexia, nausea, vomiting, vertigo, dizziness or tremors. Caution is advised in cases of impaired kidney function or severe hepatic damage.

DOSAGE: Recommended dosage is 15 mg. per Kg. per day divided into three doses, given for 7 consecutive days.

PREPARATIONS: Tablets containing 0.2 Gm. Lucanthone hydrochloride.

PACKAGING: Bottles of 30 tablets.

SUPPLIER: Burroughs Wellcome & Co.

Medrol with Orthoxine

COMPOSITION: Methylprednisolone (Medrol) and methoxyphenamine (Orthoxine) hydrochloride.

INDICATIONS: Combines anti-inflammatory effect with bronchodilating action; for use in moderately severe to severe bronchial asthma and allergic rhinitis.

SIDE EFFECTS AND CONTRAINDICATIONS: May include nervousness, epigastric distress, insomnia, moon facies, urinary frequency, nocturia and dysuria. Should not be used in patients with arrested tuberculosis, peptic ulcers, acute psychoses, Cushing's syndrome, herpes simplex keratitis, vaccinia and varicella. Should be used with caution in diabetes mellitus, osteoporosis, etc.

DOSAGE: One tablet 3 or 4 times daily.

PREPARATIONS: Tablets containing methylprednisolone 2 mg. and methoxyphenamine hydrochloride 75 mg.

PACKAGING: Bottles of 30 and 100 tablets.

SUPPLIER: Upjohn Co.

Triurate

COMPOSITION: Zoxazolamine (Flexin), colchicine, and acetaminophen (Tylenol).

INDICATIONS: In chronic gout and gouty arthritis for reduction of serum uric acid levels and for prevention of flare-ups of acute gout.

SIDE EFFECTS AND CONTRAINDICATIONS: Not recommended for treatment of acute gout. Occasional patients may note nausea, dizziness, drowsiness, and urticaria or other allergic-type skin eruptions.

DOSAGE: One tablet 3 times daily after meals. Patients should be instructed to ingest 2 full glasses of liquids with each meal and two full glasses of liquids between meals.

PREPARATIONS: Tablets containing zoxazolamine 100 mg., colchicine 0.5 mg., and acetaminophen 300 mg.

PACKAGING: Bottles of 50 and 500 tablets.

SUPPLIER: McNeil Laboratories.

THE LAW
of hospital pharmacy

edited by GEORGE F. ARCHAMBAULT

► *Because law is a complex specialty made so because of the existence of a set of Federal laws, 50 sets of state laws, and many county and municipal laws and regulations, the author of the column strongly recommends that when specific legal questions arise, one should always consult an attorney, competent in the local law.*

Are Trade Names For Single Drug Entities and "Official" Preparations Really Necessary To Insure Quality Drugs?

► SOME 30 OR 40 YEARS AGO THE DRUG INDUSTRY, in seeking techniques to acquaint physicians of the country with their ethical medication specialties (which had come of "age"), adopted the two typical approaches used in modern-day merchandising promotion: (1) Promotion with emphasis placed on *house quality* such as Triple Bromides Effervescent (*B.W. & Co.*); Mineral Oil, Squibb; and (2) promotion based on the use of trade names, for example, "Argyrol." The latter technique, obviating the use of house or firm designation on the written prescription, has become in recent years, the more popular in the merchandising of pharmaceutical specialties. Unquestionably, this is a sound and probably the only, sensible approach for true specialties, that is, those medications that contain *several active ingredients and that have no official U.S.P. or N.F. titles.*

However, many in the medical and pharmacy professions, believe the drug industry makes a serious mistake in permitting the trade name philosophy to be the advertising and sales promotion technique for pharmaceutical specialties of *single drug entities and official preparations.* They believe the house quality designation to be the better approach.

The food industry has used the "house quality designation" with considerable success. For example, "tomato soup" in the grocery stores and supermarkets remains even today (1960) simply "tomato soup." The customer is taught, through intensive advertising and merchandising to demand "Campbell's" or "Heinz" or other quality brands.

How much more sensible is this "house quality" approach in the merchandising of the *single drug entity medications,* than the present nomenclature that resorts to several trade names (nicknames as some claim) for the same drug.

More than just a few in the health care professions believe that the trade name approach is outdated because, among other things, it is gradually but surely making a mockery of the official titles and synonyms of the *U.S.P.* and *N.F.* and the scientific and nonproprietary drug nomenclature of medicine and science. These nonproprietary or "generic" names, because of the great emphasis now placed on trade names, might be likened to words in a dead language such as Latin. They are seldom used by many in today's commerce of drugs, and in the interflow of "language" among prescribers (physicians), dispensers (pharmacists) or in the administration of drugs (nurses) except in those circles that cling to the precise language of scientific drug nomenclature.

Our medical, dental, pharmacy, nursing and other health profession schools spend four or more years teaching standard drug nomenclature, as used in the official national and international pharmacopeias, and the medical and pharmaceutical literature. Their efforts, we know, are greatly diluted or lost within the first few years of the professional's practice because of the impetus given trade names in daily communications by the drug house mailing pieces and the "details" of the medical sales representative.

One witness at the Kefauver hearings stated, "The *U.S.P.* label (meaning official nonproprietary titles) gives no assurance of potency." How often have we been told by some medical sales representatives that *"U.S.P.* means *minimum passing quality,"* or *"U.S.P.* tolerances are so wide as to be meaningless," or that "Product X is superior to the *U.S.P.* item." This type of loose talk, if taken seriously, may well lead to the disappearance of our highly respected *U.S.P.* and *N.F.* as reference standards in the years ahead. This would be, we all agree, I'm sure, a great disservice to the

American people and to American pharmacy. All pharmacists know that *U.S.P.* standards are so stated so as to set a "minimum and up" quality level. The minimum indicates a level or floor of quality below which a drug must not fall. Drugs that exceed this "minimum" standard for purity, are still *"U.S.P."* and of course *do not* exceed the U.S.P. quality (see General Notices pertaining to *U.S.P.* standards). Also, drugs at the "floor" level are excellent drugs or the *U.S.P.* officials and experts would never have allowed the floor of the standard. The same applies to the *N.F.*

A physician under the "house designation" approach, it should be noted, may, if he wishes, indicate on his prescriptions or orders, a particular firm's product. He does this by specifying the house or firm along with the writing of the official or nonproprietary name. This right of "house designation" is a right we all respect. By the same token, many physicians rely on the professional judgment of the pharmacist in selecting the source or manufacturer of a drug. This is especially true in hospital pharmacy practice. It is a responsibility we accept and discharge with full recognition of the trust placed in the profession by medicine. We do not need trade names *per se* for it is our business to know the quality houses, large and small, of the country.

To make our point that the "house quality" or the "house designation" route has much to offer the individual drug producer of quality products, note that the Food and Drug Administration records indicate that during the past 10 years the Food and Drug Administration took action against the 28 firms producing 87 percent of the nation's drugs but four times (a wonderful record). As an aside, we note that approximately 1,200 smaller firms that produced the remaining 13 percent of the nation's drugs were cited 484 times (235 firms involved). The Food and Drug Administration asked (and was denied) in 1953 for the licensing of drug firms (most community pharmacies and all pharmacists have been licensed and properly so for years). This was a reasonable and proper request, one made in the interest of the public health for the evidence here cited indicates the problem of substandard drugs is not a problem in drug standard enforcement. Firms large or small, operating properly, certainly have nothing to fear from such legislation.

From the evidence now in, relative to the substandard quality of drugs and medications in commerce, as brought out by the drug industry at the "hearings," one recognizes the seriousness of the situation and the fact that the time has now arrived when physicians, pharmacists and the public alike must be guaranteed that *all* drugs (prescription or otherwise) are safe, effective, of the strength claimed and free from adulteration.

Senate Bill 3815 and House Bill 12949 introduced July 2, 1960 in Congress tend to correct the present situation—these bills are designed "to protect the Public health by amending the Federal Food, Drug and Cosmetic Act so as to clarify and strengthen existing inspection authority thereunder; require manufacturers of new drugs to keep records of, and make reports on, clinical experience and other relevant data bearing on the permissibility of such drugs; require that drugs be prepared or packed under adequate controls to insure proper identity, strength, purity, and quality, and otherwise insure their compliance with the Act; and extend to all antibiotics the certification and provisions of the Act now limited to certain antibiotics." (This Act may be cited as the Federal Inspection and Drug Amendments of 1960.)

Interpreters of these bills claim that the language is broad enough to include inspection of prescription files of local pharmacies though intended for manufacturing plants. Pharmacists, as individuals, keenly interested in the public health, will have no objection to this inspection feature of the Bills. They recognize its need as they recognize a similar need in the Harrison Narcotic Act.

Returning now to the trade name-nonproprietary name discussion, someone no doubt will cry, the adoption of the "house designation method" of merchandising will destroy the American way of doing things, a part of the American way of life—the value of trade names. In all seriousness, hasn't the use of trade names for drug products really destroyed a very old and wonderful part of the American way of life in medicine and pharmacy—the respect and knowledge the practitioners of medicine, dentistry and pharmacy once had for U.S.P. and N.F. medications, their titles and their standards? Many in the professions would like to see a return to the American way of life that medicine and pharmacy are losing through trade name practices for *single drug entity and "official" medications.* These individuals, by and large, are believers in trade name advertising *where the consumer selects the item,* but such, it should be noted, is not the case in this instance. Physicians and pharmacists do not need trade names. It is an affront to their professional reputations to claim nonproprietary names are too cumbersome for their use, although I agree such names should be shortened and made more pronounceable.

A major change in this direction in drug merchandising, by the drug industry, would be a real contribution to the health professions. It would aid the professions in maintaining and strengthening the use of scientific drug terminology as taught to the embryonic physician, pharmacist and nurse in our medical, pharmacy and nursing schools.

Those seeking a fairly up-to-date trade name-generic name listing may write to the American Pharmaceutical Association for a copy of *Proprietary Names of Official Drugs* (formerly known as Manual 102). The Amer-

ican Pharmaceutical Association has made a real contribution in attempting to eliminate, through this brochure,* some of the confusion between trade and nonproprietary names, including the *U.S.P.* and *N.F.* official drug titles. The *American Drug Index* by Wilson and Jones is another excellent listing, one that is kept current annually. Each nursing station in a hospital should, in my opinion, have a copy of one or the other along with a copy of the hospital's formulary.

Hospital pharmacists working with medical record librarians in the new Federal Food and Drug Reporting of Adverse Drug Reactions Program, should in addition to these references, be familiar with the *nonproprietary nomenclature* used in the section "Adverse Effects of Chemical Substances" (p. 151-163) of the "Diagnostic Index . . . International Classifications, U.S. Public Health Service 1959." This document is available from the Superintendent of Documents, U.S. Government Printing Office, Washington 25, D. C. for $1.00. This section also helps alleviate confusion surrounding the nonproprietary-trade name problem in medical, pharmacy, nursing and hospital communications, especially in hospital medical records.

We close with these thought-provoking quotes from President Trygstad's remarks in his recent "As the President Sees It" column, the December 1959 Dallas, Texas A.M.A. Report and the A.Ph.A. Constitution:

"A.Ph.A. Resolution (1955)

> *Whereas,* it is agreed by all pharmaceutical authorities that generic names mean the common, chemical, or unregistered names of drugs, or the names recognized by the U. S. Pharmacopeia, the National Formulary, or the Homeopathic Pharmacopoeia of the United States, or the names adopted by the Council on Pharmacy and Chemistry of the American Medical Association, and *Whereas,* the use of generic names is, therefore, in keeping with the highest ethical standards of the medical and pharmaceutical professions,
>
> Be It Resolved, that the American Pharmaceutical Association, as such, believes in and encourages the use of generic names for general drug products.

The Council directed the Secretary to publicize this resolution. (*J. Am. Pharm. Assoc., Pract. Pharm. Ed. 16*:365 (June) 1955.)

A.Ph.A. Resolution (1956)

> Resolved, that the American Pharmaceutical Association support and encourage the use of generic names in the prescribing and dispensing of drugs by the medical and pharmaceutical professions.

The House of Delegates approved this resolution as a reiteration of the official stand of the Association on this subject. The Council directed the secretary to publicize the resolution (*J. Am. Pharm. Assoc., Pract. Pharm. Ed. 17*:302 (May) 1956.)

The foregoing resolutions, adopted in 1955 and 1956, represent the official position of our parent organization, the American Pharmaceutical Association, and to my knowledge, have not been altered or rescinded by an official action of the Association.

The following report was adopted by the House of Delegates of the American Medical Association at its recent meeting.

> *"Supplementary Report C, Council on Medical Service, Drug Costs for Welfare Recipients*—Your reference committee studied Supplementary Report C of the Council on Medical Service and listened attentively to the comments made at the reference committee hearing.
>
> "First of all, your reference committee would respectfully urge full and complete cooperation by members of the Association with the *American Public Welfare Association* in its study relative to the rising costs of drugs in welfare medical care programs.
>
> "Secondly, pending the completion of this or any other study, the reference committee would urge members of the Association to be cognizant of this matter. *Physicians might well give consideration to prescribing by generic rather than trade names;* they might seek knowledge of the relative costs of comparable drugs and they might give consideration to the more frequent use of accepted drug products of reasonable cost in the treatment of welfare patients."

Constitution—American Pharmaceutical Association

"Article II—OBJECTS

> The Association shall unite for the following purposes.
>
> 1. To improve and promote the public health by aiding in the establishment of satisfactory standards for drugs, *and to aid in the detection and prevention of adulteration and misbranding of drugs and medicines,* and to take such steps as an *Association* and in cooperation with other organizations as will assure the production and distribution of drugs and medicines of the highest quality."

While the stated objectives of the ASHP make no direct reference to the quality of drugs and medicines, by its very application with the A.Ph.A., we, along with all other practitioners of pharmacy belonging to the American Pharmaceutical Association, are pledged to work for these standards in the interest of the public health.

And so—the query is asked "Are Trade Names for single drug entities and official preparations really necessary to insure quality drugs for the American people?"

**Proprietary Names of Official Drugs* has recently been sent to every member of the American Pharmaceutical Association. Single additional copies are available at 25 cents each. Quantities of from 10 to 99 are available at 15 cents per copy, and quantity purchases for 100 or more can be obtained at 10 cents per copy, postage prepaid. Orders should be sent to the American Pharmaceutical Association, 2215 Constitution Ave., N. W., Washington 7, D. C.

Consulting WITH BOWLES

GROVER C. BOWLES JR., *Baptist Memorial Hospital, Memphis, Tennessee*

► Please list some preservatives that may be used in multiple-dose injectables and indicate the concentration of each that should be employed.

Care must be taken in selecting preservatives for parenteral preparations. The agent must be chemically and therapeutically compatible with the other ingredients. The preservative must not add to the instability of the product and it must be harmless in the amounts normally administered to patients. No preservative should be added to large volume intravenous fluids.

Here are some bacteriostatic agents that may be used in the preparation of small volume injectables:

Chlorobutanol, U.S.P., anhydrous	0.33%
Phenol, reagent grade	0.4 % – 0.5%
Cresol, reagent grade	0.25%
Benzyl Alcohol, reagent grade	1.5 %

Methylparaben, U.S.P. 0.18% with Propylparaben, U.S.P. 0.02% (The parabens should always be used together. Generally the proportion is 9 parts of the methyl ester with 1 part of the propyl ester.)

Other bacteriostatic agents include the mercury compounds and cationic surfactants.

► When the chief pharmacist is lazy, uncooperative and against starting anything which might improve our pharmacy service, do you feel the assistant chief should take it upon himself to start improvements such as teaching the student nurses, trying to activate a dead Pharmacy and Therapeutics Committee, working on a formulary and many other things?

No. If things are as bad as your statement indicates—find yourself another job where they not only want and appreciate good pharmaceutical service but demand it.

► Where can you buy a 5000 ml. graduated flask?

Graduated cylinders, 5000 ml. and 10,000 ml., are available from Ace Glass, Incorporated, Vineland, New Jersey. These cylinders are graduated in subdivisions of 100 ml. and are suitable for batch operation and mixing large volumes of measured liquids.

► What is the hospital pharmacist's responsibility to his state pharmaceutical association?

The hospital pharmacist has a professional obligation to belong to his state pharmaceutical association and to take an active part in their activities—*provided* he is accorded the privilege of full membership with voting rights.

► Where can we obtain a copy of the Federal Narcotic Law?

I. R. S. Publication's No. 428 (6-59), more commonly known as Regulation No. 5, is available from the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C. The price of this publication is 35c.

This publication contains the joint narcotic regulations made by the Commissioner of Narcotics and the Commissioner of Internal Revenue with the approval of the Secretary of the Treasury, relating to the importation, manufacturing, production, compounding, sale, dealing in, dispensing and giving away of opium, coca leaves, isonipecaine or opiates and any of their compounds, derivatives or preparations.

► Should the Department of Pharmacy furnish the Outpatient Department with a price list of the commonly prescribed drugs?

I see no reason not to furnish such a list. Certainly, the intern, resident and young physician need to know something about the cost of drugs to the patient. Obviously, such a list should be limited to the most frequently used drugs and should be revised frequently. It might also be well to include a carefully prepared introductory statement such as:

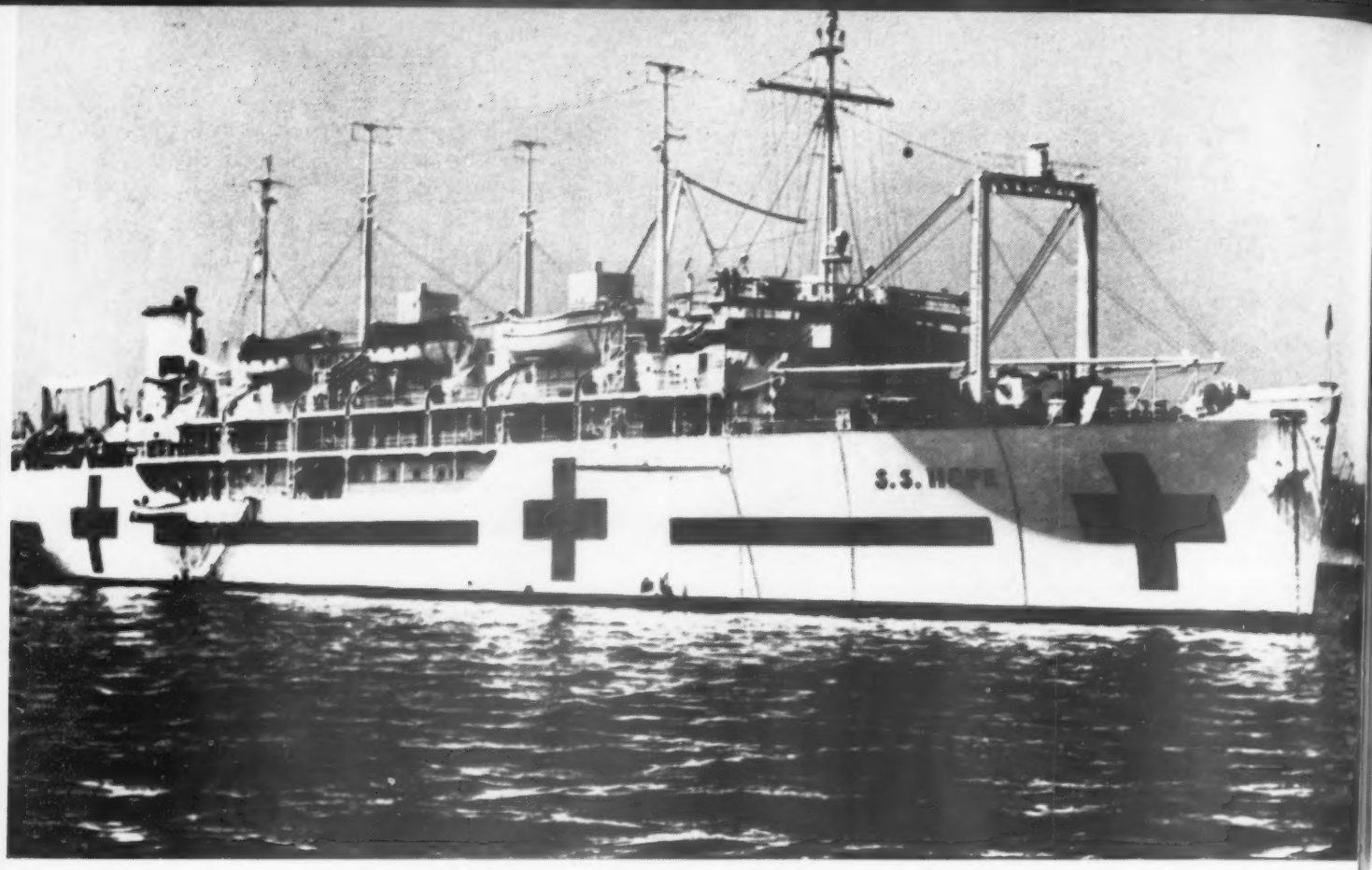
"This list, which gives the approximate cost to the patient of some frequently prescribed medications, has been compiled for your information. In using this list, bear in mind that the price of a prescription will vary from pharmacy to pharmacy and from community to community. The cost of drugs, like the cost of other items in the family budget, is increasing. Thus, at best, this list can be used only as a rough guide as to the patient cost for the items listed.

"For simplicity, the list is arranged alphabetically by the nonproprietary or generic name and no attempt has been made to list all items prescribed in the Outpatient Department. We hope that you will find this information helpful and that you will feel free to telephone the Pharmacy for additional information about the drugs when needed. You are also welcome to use the reference facilities in the Pharmacy at any time.

"Your suggestions for improving the pharmacy service in the hospital and the Outpatient Department are most welcome."

► Can we legally use narcotics from the hospital stock for laboratory purposes?

No. Narcotic drugs for use in a laboratory for the purposes of research, instruction or analysis, must be obtained under a Class VI registration.



► THE GOOD SHIP HOPE, formerly the U.S.S. Consolation, will depart San Francisco in September to serve as a 230-bed floating medical center and school, carrying to millions in Indonesia and other Asian countries new knowledge of modern methods for the diagnosis, prevention, and treatment of diseases.

Vernon O. Trygstad (l.), President of the ASHP, presents a copy of the American Hospital Formulary Service to John I. Spreckelmyer (r.), Administrator of the hospital ship "S. S. HOPE" which will tour the world as a part of Project HOPE

The money to finance HOPE is being raised by private contributions from business, industry, labor and private individuals. The government's only role is the loan of the hospital ship, which will be operated by the American President Lines at cost. The cost of the first year's operation for the project is estimated to be about $3.5 million.

"This is an attempt to do privately the kind of thing that is usually done by governments," says Dr. Willam B. Walsh, Director of the Project and President of the People-to-People Health Foundation.

"We've received contributions from cities and towns all over the country—everything from nickels and dimes from children to thousands of dollars by major companies. The pharmaceutical companies are donating the drugs, oil companies are underwriting the fuel costs. Labor unions are contributing. But we still need money," says Dr. Walsh.

Support for Project HOPE is widespread. The American Medical Association and the American Dental Association have not only endorsed the project but also made sizable contributions to it. Other groups have contributed services and material as well as money.

According to Dr. Walsh, Project HOPE is no panacea. His comments in the following paragraphs indicate the overall objectives of the Project:

Project HOPE'S doctors will work in teams with local physicians when the S. S. HOPE visits Southeast Asia

HELP LAUNCH HOPE

"We recognize that no single ship and a small staff of medical people can bring about major changes in an area where health conditions are so poor. That's why our emphasis will be on training, rather than treatment. It will take many more years, many more people and a lot more money to bring about an appreciable change in the overall health conditions of the newly developed countries.

"We believe HOPE can become a dramatic example of what can be done by private individuals, business and labor to aid less fortunate people.

"If we continue to obtain this broad support of Americans, HOPE can be the forerunner of more widespread training operations that may eventually lead to establishment of permanent installations as these countries are able to staff them with their own people."

Contributions for Project HOPE are tax deductable and may be mailed to P.O. Box 9808, Washington 15, D. C.

See also page 473 for an account of the professional objectives of this project.

Dr. William B. Walsh, shown with a model of the S. S. HOPE, is president of The People-to-People Health Foundation, sponsor of Project HOPE

HELP LAUNCH HOPE
PROJECT HOPE WILL BRING AMERICA'S MODERN MEDICAL KNOW-HOW TO THE DISEASE-RIDDEN, NEWLY DEVELOPING COUNTRIES OF THE WORLD. HOPE IS A PEOPLE-TO-PEOPLE PROGRAM. AMERICAN DOCTORS, NURSES, TECHNICIANS WILL WORK HAND-IN-HAND WITH THE LOCAL HEALTH PEOPLE.
Gretter
S.S. HOPE
WITH YOUR HELP, THE SS HOPE WILL SERVE AS A FLOATING MEDICAL TRAINING CENTER. FIRST STOP: INDONESIA, WHERE THERE ARE 71,000 PERSONS FOR EACH DOCTOR... COMPARED TO ONE DOCTOR FOR EACH 750 PERSONS IN THE U. S.
YOU CAN HELP BRING HEALTH OPPORTUNITY FOR PEOPLE EVERYWHERE...
SEND YOUR CONTRIBUTION TO PROJECT HOPE
P.O. BOX 9808
WASHINGTON 15, D.C.

GEORGE URDANG

AS MY TEACHER AND COLLEAGUE

an invitational comment offered at his funeral June 29, 1960

by GLENN SONNEDECKER

► ANYONE WHO KNEW GEORGE URDANG well enough to be invited to remind others of his merits on this unhappy day is not in an enviable position. Much that is important to convey cannot now or henceforth be conveyed. He has left us much; but with his own leaving much is gone that cannot be retrieved, that cannot be conveyed by others.

I speak of course of his *human* qualities. His *scholarly* qualities and writings are more tangible, more measurable, and more widely recognized. These are not to be minimized, because few in pharmacy—even internationally—have applied a mind and pen of such refinement to the humanistic study of the pharmaceutical profession. Yet, thinking at this moment of what has gone out of our lives, as his colleagues and students, I feel with renewed intensity the importance of a scholar as a man . . . someone who is not only paid to think, but to be thoughtful . . . someone who respects scholarship for its own sake, but who hopes his expertness somehow may also serve an ordinary man's purposes, if only his purposeful illusions. George Urdang was that kind of scholar. This personal quality cannot survive his own personality but it can continue to inspire us to try to express through our own lives some analogy of that noble fusion of intellect and emotion.

What Dr. Urdang gives to the world of pharmacy and to all who knew him sprang from a generous natural endowment, an unusual education, and a life experience that was on occasion as severe and challenging as it was rich and varied.

His natural endowment included the longest and most reliable memory that I have ever known at first hand, and an almost compulsive bent for seeing in particulars an example of the general or a part of some more meaningful whole. His natural gifts were burnished by the rigorous demands of a classical secondary schooling, followed by the scientific discipline of phar-

GLENN SONNEDECKER succeeded Dr. George Urdang as Director of the American Institute of the History of Pharmacy, Madison, Wisconsin.

Dr. George Urdang as he delivered the principal address at the Decennial Banquet of the American Society of Hospital Pharmacists, Philadelphia, August 22, 1952. Dr. Urdang was helpful during the writing of "Ten Years of the ASHP" which was published at the time of the meeting marking the Society's first decade

maceutical studies in the University of Leipzig. Later he infused this background with doctoral studies in the historical and economic ramifications of his chosen profession of pharmacy.

He was a pharmacist first of all, not only in his career, I believe, but always so in his thought. After nine years as a pharmacy owner and spare-time author, he went to Berlin as an editor of one of Germany's most influential journals of pharmacy. As his experience and knowledge matured, his pen was attracted increasingly by the depth and diversity of history. Facile as well as meaningful in speaking as in writing, he soon came to prominence. Dr. Urdang's subsequent historical work formed both a foundation and a pattern for some of his publications and organizational work later on in America.

Here I learned to know him at the full maturity of his powers. Between 1948 and now, I have had the privilege of close association with him, first as a graduate student and then as his successor at the University. Thus it happened, at many unguarded moments, that I saw naked his emotions and his thought and his conduct. At such moments, when so many men of presumed importance shrivel before your eyes, Dr. Urdang seemed to grow in stature.

He had an unfailing dignity that he bore with ease and lack of pretense. He had a kindness so spontaneous and deep-going that it was never over-run by the inevitable busyness of a life so full. He had an unqualified conviction of the worth in every human being and every honest endeavor—without pretending that evil is virtue. By encouragement and ennoblement of more modest efforts than his own, adjuring any vain display of critical acuity or ridicule, he placed a lasting and constructive influence upon many lives and events.

After becoming a world renowned scholar, he remained alert to every small opportunity to help someone understand and fulfill his intellectual or human potential. In the quiet voice of such spirit—perhaps as much as in the authoritative voice of his historical scholarship—Dr. Urdang has been saying something that is not only important to us in pharmacy but to the world.

GEORGE URDANG

world renown historian of pharmacy, dies at 78

► GEORGE URDANG died Monday, June 27, 1960, in Madison, Wisconsin at age 78, after a career that had earned him international recognition as one of the greatest pharmacist-scholars ever to devote his talent to the study and writing of pharmacy's history. He reached retirement age eight years ago at the University of Wisconsin, where he was the first full professor in the history of pharmacy. Since then his professional activities had been progressively curtailed by parkinsonism. Three years ago he also retired as Director of the American Institute of the History of Pharmacy.

Born at Tilsit, Germany (13 June 1882) Dr. Urdang had been in the United States since 1938. Educated as a pharmacist at the University of Leipzig, he practiced pharmacy for nine years in Rosenberg, West Prussia. Already at this time his contributions to journals of pharmacy and other publications made him widely known. In 1919 he was appointed editor of the well-known German journal, the *Pharmazeutische Zeitung*, a position he held until the political uproar in Nazi Germany forced his resignation.

Urdang had taken up advanced historical and social studies, meanwhile, at the Universities of Berlin and Halle-Wittenberg, earning the degree of Doctor of Natural Science "with distinction." He was the first in Germany to receive such a degree on the basis of a historical thesis with pharmacy as a major. He also was the only one to receive his degree under the world-famous historian of science, E. von Lippmann.

In 1926 Urdang founded, together with four friends, the German Society for the History of Pharmacy, which he served as director until 1934. After World War II, the Society made Urdang an honorary member and awarded him the Schelenz Plaque in 1949, the same year in which he received the Urban Medal and the Günther Schmid Medal. Here in America he received an honorary Doctor of Science degree from the Philadelphia College of Pharmacy and Science (1946); he was selected for the J. Leon Lascoff Award (1951) by the American College of Apothecaries; and he had been an honorary member of the American Pharmaceutical Association since 1932. Honorary or corresponding memberships were accorded him by a variety of organizations in various parts of the world.

After arriving in the United States in 1938, Urdang took special studies to become licensed in America as a pharmacist; then accepted an invitation from Professor Edward Kremers at the University of Wisconsin to join him in writing the volume, History of Pharmacy, which subsequently became a standard reference and text book in the field.

Under the influence of Urdang, and based upon his experience in the German society, an American Institute of the History of Pharmacy was founded in 1941, with headquarters in Madison and with Urdang as its first Director, a position he held until 1957. During his administration the Institute became one of the most productive and best-known specialized historical societies of its kind in the world.

In 1947 the University of Wisconsin created a chair for the history of pharmacy, with Urdang as the first occupant. Until he reached retirement age (1952) at the University, Urdang gave pharmacy students, through his teaching, a strong sense of their professional heritage and a keen awareness of their place in society and the health field, according to faculty colleagues. He educated the first three men ever to obtain the Doctor of Philosophy degree in the United States on the basis of historical studies and research in the pharmaceutical field; and he helped to give recognition and leadership to a type of scholarship in the sciences and scientific professions that has since made the history of science department at the University of Wisconsin one of the outstanding centers of its kind internationally, according to historians.

Urdang wrote a number of books and scores of articles that reveal and interpret many historical developments and contributions in the field of pharmacy. His conviction that "sense finding must follow fact finding," and that every student and every human being needs to be recognized and encouraged for whatever merit he has, were firmly held ideas that gave him affection as well as respect from students and colleagues alike.

Dr. Urdang is survived by his wife, Gertrude (1635 Monroe Street, Madison 5, Wisconsin); two daughters, Mrs. Robert Alfredson and Mrs. Ursula Lewis, both of New York City; five grandchildren; and one sister, Mrs. Johanna Wilk of Madison, Wisconsin.

News

Pharmacy Represented at Conference on Aging

Dr. William S. Apple, Secretary of the American Pharmaceutical Association, will be pharmacy's sole delegate on a national level at the White House Conference on Aging in Washington, D. C., January 9-12, 1961. The American Pharmaceutical Association will participate in this important Conference on the invitation of Bertha S. Adkins, Under Secretary of Health, Education, and Welfare.

A total of 2,800 delegates will attend the Conference —1,740 from the various states and territories to be named by the respective governors; 660 representing some 250 national organizations including civic, labor, business, professional, religious and fraternal groups; and 400 from the National Committee and the consultants to the Planning Committees.

Hospital Pharmacists Convene at Midwest Meeting

The hospital pharmacists' sectional meeting at the 32nd Convention of the Midwest Hospital Association held in Kansas City, Missouri, April 27 and 28, was well attended by representatives from the area states of Arkansas, Colorado, Kansas, Missouri, Nebraska, Oklahoma, and Wyoming. The presence of two national officers of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS added much interest to the meeting. ASHP President Vernon O. Trygstad spoke on "What's Ahead for Hospital Pharmacy." Sister Mary Berenice, S.S.M., Treasurer of the ASHP, participated in a panel discussion.

A.Ph.A. President Howard C. Newton participates in installation ceremonies of the Massachusetts Society of Hospital Pharmacists. Shown in photo (l to r) are George Narinian, Program Chairman; ASHP President Vernon O. Trygstad; Dean Howard C. Newton; and George Goldstein, Chief Pharmacist, Brockton VA Hospital, and host for the evening

► JOHN A. MACCARTNEY, Director of Professional Relations for Parke, Davis and Company since 1946, has recently been appointed Director of Public Relations for the world-wide pharmaceutical firm.

In his new position, MacCartney succeeds Ralph G. Sickels, who will remain with the firm in an advisory capacity until the end of this year, according to Carl Johnson, Vice-President, Advertising and Public Relations. Sickels will retire December 31, after 40 years of service in an advertising-public relations capacity with Parke-Davis. A successor to fill the vacancy created by MacCartney's appointment has not been named.

Mr. MacCartney served as President of the American Pharmaceutical Association during the 1956-1957 term. He is a member of the ASHP.

► URSULA E. HEYER has recently been appointed Chief Pharmacist at The Johns Hopkins Hospital in Baltimore, Md. Miss Heyer is a native of Germany and served a two year apprenticeship there. In this country, she studied at the University of Wisconsin School of Pharmacy receiving a Bachelor of Science Degree in 1951. From 1956-1958 she served a pharmacy internship at The Johns Hopkins Hospital and received a Master of Science Degree in Pharmacy from the University of Maryland. She later served as Assistant Chief Pharmacist at The Johns Hopkins Hospital until her appointment as Chief Pharmacist.

Miss Heyer is a member of the International Pharmaceutical Association, the American Pharmaceutical Association, AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, American Institute of the History of Pharmacy, Maryland Association of Hospital Pharmacists, Rho Chi and Phi Beta Kappa.

► DR. JOHN N. MCDONNELL, General Manager, Pharmaceutical Laboratory Division, Schieffelin and Company, has recently been named Chairman of the Board of Trustees of Columbia University College of Pharmacy. Dr. McDonnell, who has been a Trustee of the College since 1953, has been acting Chairman since the retirement of Mr. Leo Roon a year ago. On accepting the position, Dr. McDonnell anounced that plans immediately ahead involve a new College of Pharmacy building and a Pharmaceutical Institute which will rise at the Morningside Heights location of the University. Dr. McDonnell is a member of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS and is well known to this group.

"Proprietary Names of Official Drugs" Published by A.Ph.A.

The American Pharmaceutical Association has recently published *Proprietary Names of Official Drugs*, a 48-page, easy-to-use pamphlet to fill the need for an authoritative, handy reference source to identify drugs official in the 1960 revisions of the *U.S.P.* and *N.F.* by their proprietary or other trade names.

In making the announcement, A.Ph.A. Secretary William S. Apple noted that "the astounding total of 373 of the newest, most widely used and proven effective therapeutic agents are included in *U.S.P.* XVI and *N.F.* XI. Added to the many other important agents which are being carried forward from the previous editions, this can only mean that the pharmacist, more than ever before, will be consulted as to which drug brand names correspond to which nonproprietary names, and conversely which official names apply to which trade names."

Dr. Apple continued by observing that "as the recognized local authority on drug nomenclature, every pharmacist can expect that physicians, dentists, nurses, and others active in the health field will come more and more to rely upon him to provide factual, up-to-date information on new drugs. In anticipation of this need, the American Pharmaceutical Association has published *Proprietary Names of Official Drugs.* This is the second edition of the pamphlet formerly known as Manual 102."

Every member of the American Pharmaceutical Association will receive by mail a complimentary copy of this new comprehensive drug name lexicon. For others, single copies are available at 25 cents per copy. Quantities of from 10 to 99 are available at 15 cents per copy, and quantity purchases for 100 or more can be obtained at 10 cents per copy, postage prepaid. Orders should be sent to the American Pharmaceutical Association, 2215 Constitution Avenue, N. W., Washington 7, D. C.

► THE *Texas Journal of Pharmacy* is a new publication, the first issue (Vol. 1, No. 1) of which was made available in the Winter, 1960. Dean Henry M. Burlage of the University of Texas School of Pharmacy, is Managing Editor. The *Journal* is to be published quarterly in January, April, July, and October. The subscription price is $2.00 per year (domestic); $2.50 per year (foreign). Single numbers are $0.50 each domestic, $0.60 each foreign.

Of particular note to hospital pharmacists is the appearance in the first issue of a series of three lectures on hospital pharmacy by Robert C. Bogash, immediate Past-President of the AMERICAN SOCIETY OF HOSPITAL PHARMACIST. The series was presented as part of the Second Annual Visiting Lecture Series in the pharmaceutical sciences, during 1959.

American Hospital Association Meets in San Francisco

Hospital pharmacy will be represented at one of the program sessions at the Annual Convention of the American Hospital Association in San Francisco during the week of August 29. In an instructional conference dealing with "Statement of Guiding Principles on the Operation of the Hospital Formulary System," leaders in hospital pharmacy and hospital administration will discuss this important area. Participants include Mr. W. Kevin Hegerty, Administrator at Greater Bakersfield Memorial Hospital, Bakersfield, Calif., who will serve as Chairman of the discussion; Mr. Vernon O. Trygstad, Past-President of the ASHP and Director of Pharmacy Service of the Veterans Administration; Mr. Joseph Oddis, Director of the Division of Hospital Pharmacy; and Mr. Alanson W. Willcox, Legal Counsel for the American Hospital Association and with the Washington Bureau.

Also, an exhibit sponsored by the American Pharmaceutical Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS will be among the Convention's technical exhibits which is the world's largest display of hospital equipment and supplies. Assisting with this will be representatives of the Northern California Society of Hospital Pharmacists.

Convention meetings will be held at the San Francisco Civic Center with 40 program sessions and more than 400 exhibits covering all facets of hospital operation.

The 128-member House of Delegates, the A.H.A.'s policy making group, will meet Monday, Tuesday and Wednesday mornings at the Jack Tar Hotel. Russell A. Nelson, M.D., president of the AHA and director of the Johns Hopkins Hospital, Baltimore, will preside.

Induction of the new president, Frank S. Groner, administrator of Baptist Memorial Hospital, Memphis, Tenn., will take place Tuesday morning before the House of Delegates.

Program sessions will range from general assemblies covering major national issues to instructional conferences dealing with specific phases of hospital operation.

Three of the general assembly speakers will be Fred C. Foy, President of the Koppers Company, Pittsburgh, and Chairman of the Committee on Careers of the National League for Nursing, Inc.; W. Allen Wallis, Dean of the Graduate School of Business of the University of Chicago and Special Assistant to President Eisenhower, and J. Waldo Monteith, Minister of National Health and Welfare of Canada.

There will be a daily film program, as well as sessions of special interest to hospital auxiliary and volunteer members. A feature will be an idea exchange for directors of volunteers Monday afternoon.

Other special events will include:

—An auxiliary breakfast at which the speaker will be Jack Masur, M.D., Assistant Surgeon General of the U. S. Public Health Service and Director of the Clinical Center, National Institutes of Health, Bethesda, Md.

—The AHA banquet where Oliver G. Pratt, Executive Director of the Rhode Island Hospital, Providence, will receive the Association's Distinguished Service Award for 1960. In addition, honorary memberships in the Association will be presented.

—The federal hospital executives' luncheon at which the speaker will be Sumner G. Whittier, administrator of veterans affairs, Washington, D.C.

—The Catholic sisters' luncheon.

—The architectural exhibition of hospitals, which will include photos, plans, and scale models of outstanding hospitals and other health care facilities.

Several allied groups will meet in conjunction with the A.H.A. Among them are the American Association of Hospital Consultants, August 27; the American Association for Hospital Planning, August 26-27; the American College of Hospital Administrators, August 28-30, and the American Association of Nurse Anesthetists, August 29-September 1.

as the president sees it—

CLIFTON J. LATIOLAIS, *Ohio State University Health Center, Columbus, Ohio*

► I WELCOME THE OPPORTUNITY, through your official JOURNAL, to be able to communicate with you in this column during the next SOCIETY year. To those of you who were not able to attend the Annual Meeting in Washington during the week of August 14, may I take this opportunity to express my personal gratitude for having selected me to serve as your president for the coming year. Additionally, warm felicitations come from Mr. Peter Solyom, your Vice-President, Mr. Joseph Oddis your new Executive Secretary and your hard working and devoted Treasurer, Sister Mary Berenice.

Our Annual Meeting a few days ago marked the completion of eighteen years of proud history for the AMERICAN SOCIETY OF HOSPITAL PHARMACIST. For those 153 Charter Members, the struggles and problems during those formative years were many. The dynamic growth, progress and accomplishments of the SOCIETY since its meager beginnings are a tribute to these members. Their enthusiastic dedication and their struggle for professional respectability have fulfilled, to a great degree, their vision of greatness for American hospital pharmacy.

While we review the past accomplishments of the SOCIETY, so also do we see the progress which has been made in other segments of the health professions. So much so that as we embark upon this sixth decade, hospital pharmacy is faced with many challenges—challenges which must be met if we are to keep pace with the growth of dynamic America.

The SOCIETY is equipped to meet these challenges. A membership of 3,500 strong and some 54 Affiliated Chapters from every geographic location of this country provide a degree of strength and unity of purpose to tackle these challenges.

The organizational structure of the SOCIETY through its committees—standing and special, joint and liaison—provides an opportunity for extensive participation of individual members in the work of the organization. Completion of the work of the Committee to Study Re-Organization should provide an even greater opportunity for SOCIETY progress. Further, election of an Executive Secretary as an employee of the SOCIETY will provide additional avenues of service.

Liaison activities between the SOCIETY and the National League for Nursing for the past couple of years has helped materially in bringing to hospital pharmacists guidelines on safety practices and procedures relating to our professional sphere of service. The results of this most important activity may be credited to the outstanding work of our Special Committee on Safety Practices and Procedures. Thus, our next problem is to implement these guidelines in *individual* hospitals. This can be accomplished only by individuals—you and I. In other words, this is a two way street. Individuals make up the SOCIETY. As individuals, we bring matters to the attention of the SOCIETY—problems which usually can best be solved through united effort on a national basis. Solution of the problem through SOCIETY action leads us to the implementation aspects which must go back to the individual. And, once this has been accomplished we can truly claim that progress has been made.

There are many other projects which have gone up the organizational scale; solutions to these problems have been obtained; they have been referred back to us as individuals for implementation. Some examples of these are: (1) Principles Involved in the Use of Investigational Drugs in Hospitals; (2) Statement on the Pharmacy and Therapeutics Committee; (3) Statement of Principles in the Operation of the Formulary System; (4) Establishment of Liaison Committees between State Hospital Associations and State Hospital Pharmacy Societies and State Boards of Pharmacy, etc. Each of these areas has been designed to assist in elevating certain facets of pharmaceutical service which is part and parcel of a dynamic health care program. Thus, each of us is challenged to follow through by implementing these programs.

While there is no rest for the weary and we, individually, are working on these programs, the SOCIETY collectively, is toiling on other problems. When our present activities are completed, these SOCIETY programs will be in their final stages of development and ready for implementation. This is our cycle of progress. Shall we, as we enter the "Challenging Sixties," keep this cycle on the move?

At the April, 1949 Convention in Atlantic City the House of Delegates elected a new Secretary of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS. For eleven years the SOCIETY has been eminently rewarded with outstanding service and unswerving devotion to duty from its Secretary. Her voluntary contribution of time without financial compensation for her services to hospital pharmacy during this decade plus is exemplary. True, perhaps in 1949 SOCIETY activities were not so complex; yet during the past few years it has warranted practically her full time attention. Probably no one knows more fully the tremendous job the Secretary has performed during this period than those individuals who have served as President of the SOCIETY with her. It was Sir Francis Bacon who said, "I hold every man a debtor to his profession." No one in hospital pharmacy today has paid his debt to his profession more fully than *Gloria Niemeyer Francke*. We in the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS shall always owe our debt to "Gloria." While she has relinquished her responsibilities as Executive Secretary of the SOCIETY during this past Annual Meeting, she continues her work in varied activities including the Associate Editorship of the AMERICAN JOURNAL OF HOSPITAL PHARMACY. Won't you join me in wishing 'Gloria' Godspeed?

The AMERICAN SOCIETY OF HOSPITAL PHARMACIST is extremely fortunate in having elected as its new Executive Secretary a most dedicated, enthusiastic and astute hospital pharmacist—Mr. Joseph A. Oddis. The responsibilities of his office are many and his services are varied—to the President and the other SOCIETY Officers, to the Executive Committee, to the House of Delegates, to Affiliated Chapters, to the membership collectively and individually, to the other segments of the profession through their respective organizations, to hospital and other related health organizations, etc. Each of these individuals and groups at some time or other expects services of some type from the Secretary of the SOCIETY. I am sure you will agree that his is a most difficult task. Yes, it seems that we do expect very much from the office of the secretary. On the other hand, it would seem that the Secretary should expect much from you and I as individual members, as delegates and representatives of Affiliated Chapters, etc. if he is to provide the services which we expect. Join with me and give him your support for a better and stronger AMERICAN SOCIETY OF HOSPITAL PHARMACIST.

Many of you were not able to attend the Annual Meeting and perhaps have not at some time or other had the opportunity of meeting Mr. Oddis personally. I hope you will have this opportunity soon. In the meantime, I have asked him to address a personal communication to all of you in this column of the next issue.

CLIFTON J. LATIOLAIS

First Specialized Institute

► THE FIRST SPECIALIZED INSTITUTE ON Hospital Pharmacy will be presented at the American Hospital Association Headquarters Building, Chicago, Illinois, on October 12-14, 1960. Following the traditional pattern established for holding general institutes, the Specialized Institute will be conducted by the AHA in cooperation with the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS and the American Pharmaceutical Association.

This being the first institute of this type to be held for hospital pharmacists by the participating organizations, the central theme of "hospital pharmacy administration" was selected for study in depth. Although problems of organizational communication will serve as the focus for the general theme of hospital pharmacy administration, it is anticipated that such factors as organization and administration, supervision, planning and scheduling, problem solving, etc. will be included in the three day session.

This institute is designed to help pharmacists with administrative responsibilities deal more effectively with communication difficulties by providing:

—knowledge of relevant theories of the communication process;

—understanding of both the interpersonal dimension and the role of organizational structure in modifying the adequacy of communication; and

—insight into the skills which people in organizations need to develop to carry out their professional and administrative roles most effectively.

The design of the institute utilizes *demonstrations, role playing, and small group discussion,* providing opportunity for the widest participation possible with a large group.

There will be some theory sessions, but the majority of the sessions will demand more active participation than is customary in the general institutes provided for hospital pharmacists.

Dr. Harry Miller of the Center for the Study of Liberal Education for Adults, Chicago, Illinois, has been engaged as a consultant in the planning and conduct of the institute. Assisted by a selected group of experts, he will assume a major role in relating administrative processes to hospital pharmacy departments.

Those wishing to attend must be hospital pharmacists. In addition, qualification for attendance must be determined by each prospective applicant after carefully reviewing the announced program. In arriving at a decision, each individual should consider such factors as a) attendance at previous general institutes, b) length of experience and previous positions held, and c) current position.

ABSTRACTS OF PAPERS

presented at the 19th International Congress of Pharmaceutical Sciences of the International Pharmaceutical Federation Zurich, Switzerland, September, 1959

A series of abstracts presented at the 19th International Congress of Pharmaceutical Sciences of the International Pharmaceutical Federation is appearing in THE JOURNAL. The first of the series were those presented in English and appeared in the January issue. In the second series appearing in March, the English abstracts were continued and the beginning of those translated from the German were included. A third series concluding the German abstracts appeared in the May issue. Beginning in this issue is the fourth series which includes abstracts translated from the French.

ANTHRAQUINONE CHROMATOGRAPHY

Separation and Determination by Direct Electrophoresis on Paper and by Counter-current Distribution of Anthraquinones from Official Rhubarb, (Séparation et dosage par électrophorèse continue sur papier et par répartition à contre-courant des anthraquinones de la rhubarbe officinale), by G. M. Nano, Institute di Chimica Farmaceutica e Tossicologica dell'Università, Turin, Italie.

The separation of a mixture of anthraquinones from official rhubarb has been effected by direct electrophoresis on paper and by counter-current distribution. The constituents of the extract are completely separated by direct electrophoresis on thin paper; for this it is necessary to use basic buffers (sodium borate in particular). It is also possible to separate two tannins.

A very good separation of anthraquinone compounds, even with 50 elements can be obtained by counter- current distribution between toluene or chloroform and a fixed phase accompanied by a phosphate buffer using the Craig apparatus. This separation is also good from a quantitative point of view.

By using ethyl acetate/water buffered at pH 4 it is also possible to separate the glucosides and the tannins which are present.

ARSENIOUS ANHYDRIDE CAPSULES

The Behavior of Arsenious Anhydride in Medicinal Capsules, (Le comportement de l'anhydride arsénieux dans les capsules médicamenteuses) by C. Stainer and C. L. Lapière, Institut de Pharmacie, Université, Liège, Belgique.

Examination of an anthelmintic preparation for veterinary use has shown that arsenious anhydride could be rapidly produced in the gelatinous coating of capsules. The contents of the capsules consisted of arsenious anhydride, magnesium sulfate, Istizine, carbon tetrachloride, carbon disulfide and castor oil. The arsenic was measured in the contents of the capsule and in the coating by using the Schulek method.

Analysis of identical preparations has permitted the following of the course of the phenomenon in which the following percentages of arsenic were found in the coatings: after 5 days, 6%, after 1 month 5%, and after 4 months 80%.

PHOTODYNAMIC ACTION OF RIBOFLAVIN

Study of the Photodynamic Action of Riboflavin on Bacteria, (Etude de l'action photodynamique de la Riboflavine sur des bactéries) by J. Dony and B. L'Hoest, Service de Contrôle des Médicaments de l'Association Pharmaceutique Belge, Bruxelles, Belgique.

Following the works of different authors and after personal observations of the sensitizing action of riboflavin in the photo-oxidation of various substances (antibiotics, other vitamins, amino acids, enzymes, etc.), we have verified its direct photodynamic action on living cells such as bacteria (*Klebsiella pneumoniae* and *Staphylococcus aureus*). We were able to ascertain that this action is far from negligible in the visible part of the spectrum, so that this "vitamin" can, under certain circumstances, behave as a true "disinfectant". This action has been studied with *Klebsiella pneumoniae*. On the other hand, under our experimental conditions, riboflavin protected the germ from the action of ultraviolet rays. These results are discussed on a theoretical basis and practical use of the photodynamic action of riboflavin in microbiological experiments is anticipated.

COMPARATIVE STABILITY OF PENICILLINS

A Comparative Study of the Stability of Sodium Benzylpenicillin and Phenoxymethylpenicillin in Hydrophilic and Fatty Ointments and in the Excipients for Suppositories. (Etude comparative sur la stabilité de benzylpénicilline sodique et de phénoxyméthylpénicilline dans les pommades hydrophiles et grasses et dans les excipients pour suppositoires) by E. Gradnik and F. Rota, Farmaceutici Midy, Milan, Italie.

It has been stated that phenoxymethylpenicillin, if it is incorporated in ointments with hydrophilic excipients, has no advantage over the sodium benzylpenicillin from the viewpoint of the duration of stability. On the contrary, phenoxymethylpenicillin has a stability which is superior to that of sodium benzylpenicillin in the fatty excipients used for suppositories, cocoa butter and hydrogenated oils.

MOBILIZATION OF LEAD

On the Mobilization of Lead Under the Influence of Various Medicaments, Especially the Antibiotics, (Sur la mobilisation du plomb sous l'action des différents médicaments et en particulier sous l'action des antibiotiques) by M. Mokranjac, S. Radmić and D. Soldatovic, Institut de Toxicologie, Belgrade, Yugoslavia.

The authors explain the results of their research on the effect that certain medicaments, in particular antibiotics, produce in animals and man under conditions of acute and chronic lead poisoning. Their studies have shown that the antibiotics (penicillin, streptomycin, Terramycin, tetracycline, PAS) have caused significant mobilization of lead in subjects with lead poisoning, while in normal subjects no change in the amount of lead was observed in the blood or urine. In contrast, the sulfonamides tested

have had no effect on the lead, even in subjects severely poisoned by it. It is the same with vitamin C. The authors discuss the consequences which can result from the utilization of antibiotics, and of other drugs with which they have experimented in lead poisoning.

SPARTEIN AND OXYTYRAMINE

Research on the Biogenesis of Spartein and Oxytyramine in Broom Genista (Sarothamnus Scoparius L.) by means of Lysine and Phenylalanine Uniformly Attributed to Radiocarbon C^{14}, (Recherches sur la biogenèse de la spartéine et de l'oxytyramine dans le genêt à balais (Sarothamnus scoparius L.) au moyen de lysine et de phénylalanine uniformément marquées au radiocarbone C^{14}) by F. Jaminet, Institut de Pharmacie, Université, Liège, Belgique.

Description and discussion of the results of experiments in which l-lysine and l-phenylalanine uniformly labeled with C^{14} were administered to broom genista in different stages of growth in order to discover the biogenetic processes of the plant in the syntheses of spartein and oxytyramine. It appears that lysine may be considered as the biological precursor of the nitrogen cycles of spartein. The development from lysine to spartein seems to occur through a cyclic derivative of amino acid, apparently identical to dehydropopecolic acid. In the genista, oxytyramine appears to be formed as follows:

Tyrosine $\xrightarrow[-CO_2]{}$ Tyramine $\xrightarrow[O_2]{}$ Oxytyramine

Tyrosine, precursor of oxytyramine, does not seem to be formed by hydroxylation of phenylalanine as is the case in other plants. It is suggested that the tyrosine of genista evolves from a transamination of p-hydrophenylpyruvic acid itself derived from the cyclization of hexoses.

COLORIMETRIC MEASUREMENT OF THEOPHYLLINE AND CAFFEINE

New Colorimetry for Theophylline and Caffeine, (Nouvelles colorimétries de la théophylline et de la caféine) by R. Bontemps, Service de Contrôle des Médicaments de l'Association Pharmaceutique Belge, Bruxelles, Belgique.

The author describes a colorimetric determination of theophylline with dichloroquinone-chlorimide in buffered medium as well as a determination of theophylline and caffeine with sodium hypochlorite in the presence of pyridine.

ISOSTERS OF PROCAINE

Synthesis and Action of Some Local Anesthetics, Isosteric Derivatives of Procaine, (Synthèse et action de quelques anesthésiques locaux, derivés isostères de laprocaïne) by G. Enézian, J. Enézian and J. Büchi, Institut de Pharmacie, Ecole Polytechnique Fèdérale, Zurich, Suisse.

After giving a survey of local anesthetics and developing some ideas on isosteres, we made the synthesis of some isosteres of procaine by modifying the median fraction of the molecule.

The products which were the object of our research were:

p-Aminophényl-diéthylaminoéthyl-éther $H_2N-C_6H_4-O-CH_2CH_2N(C_2H_5)_2$

p-Aminophényl-diéthylaminoéthyl-thioéther $H_2N-C_6H_4-S-CH_2CH_2N(C_2H_5)_2$

p-Aminophényl-diéthylaminoéthyl-sulfoxyde $H_2N-C_6H_4-SO-CH_2CH_2N(C_2H_5)_2$

p-Aminophényl-diéthylaminoéthyl-sulfone $H_2N-C_6H_4-SO_2-CH_2CH_2N(C_2H_5)_2$

1-(p-Aminophényl)-3-diéthylamino-propane $H_2N-C_6H_4-CH_2CH_2CH_2N(C_2H_5)_2$

1-(p-Aminophényl)-3-diéthylamino-propanol-1 $H_2N-C_6H_4-CH(OH)-CH_2CH_2N(C_2H_5)_2$

ω-Diéthylamino-p-aminopropiophénone $H_2N-C_6H_4-CO-CH_2CH_2N(C_2H_5)_2$

These derivatives formed the object of pharmaceutical experiments of which the results are given.

ANALYSIS OF LONG-ACTING SULFONAMIDES

Analytical Characteristics of Some Sulfonamides with Prolonged Action, (Caractéristiques analytiques de quelques sulfamides à action prolongée) by G. Bellomonte, A. Calò and C. Cardini, Istituto Superiore de Sanità, Rome, Italie.

The analytical characteristics of sulfonamides with retarded action, or better, with slow excretion, which have recently been introduced in therapy, have been studied.

These are: 3-sulfanilamido-6-metoxypyridazine, 3-sulfanilamido-6-chloropyridazine, 3-sulfanilamido-2-phenyl-pyrazol and 2.4-dimetoxy-6-sulfanilamido-1.3-diazine.

Particularly the spectrophotometric characteristics in U. V. and I. R. have been brought to attention and described, and the chromatographic and electrophoretic methods have been applied to the study of these compounds with the intention of characterizing and distinguishing them and of executing the determination of them in pharmaceutical preparations.

DETERMINATION OF THEOPHYLLINE

The Determination of Theophylline by Complexometry, (Le dosage de la théophylline par complexométrie), by Z. Blagojević, P. Bradic, and M. Bunović, Institut de Pharmacie Chimique, Faculté de Pharmacie, Belgrade, Yugoslavia.

In our studies we used the precipitant action of neutral copper acetate on theophylline solution in methyl alcohol. The precipitate thus formed had already been studied by A. J. Plummer and M. Péronnet and the formula established. It is a copper compound of the following formula: $(C_7H_7O_2N_4)_2Cu$, $3(CH_3COO)_2Cu$.

The precipitation was made under the same conditions as the above authors indicated. After the filtration and separation of the precipitate we measured the copper in it, as well as the excess of copper in the filtrate.

The precipitate is dissolved in dilute acetic acid and the copper is measured by complexometry, using the titrated solution 0.05 m of disodic salt of ethylenediaminotetraacetic acid (Complexon III®) in the presence of a-pyridilazo-b-naphthol (PAN) as indicator. Under the same conditions we measured the copper in the reagent used.

1 ml of titrated solution 0.05 m of Complexon III® corresponds to 0.0180 m of anhydrous theophylline.

The results obtained, whether by the measuring of copper in the precipitate, or in the filtrate, correspond to the amount of measured theophylline.

This measurement is carried out in experimental amounts of between 1 and 5 mg.

DETERMINATION OF VITAMIN B_{12}

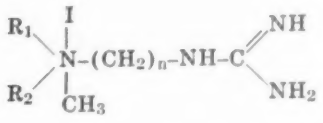
Separation of Vitamin B_{12} from Hepatic Extracts by Means of Chromatography and its Spectrophotometric Determination, (Séparation de la Vitamine B_{12} des extraits hépatiques au moyen de la chromatographie et sa détermination spectrophotométrique) by A. Mariani and C. Vicari, Istituto Superiore de Sanità, Rome, Italy.

A process has been perfected for separating vitamin B_{12} from artificially enriched hepatic extracts with the aid of chromatographic columns. A column of acid alumina is used for clearing the vitamin almost completely of the colored components of the hepatic extract. The liquid obtained by elution, which contains the whole vitamin, is passed over a second column of Florisil and vitamin B_{12} is eluated with several milliliters of 50% acetone. This process permits the extraction of the vitamin in a sufficiently concentrated solution, so as to be able to apply the spectrophotometric method for its determination.

GUANIDINES WITH QUARTERNARY AMMONIUM FUNCTION

Preparation of Guanidines also Possessing a "Quaternary Ammonium" Function (Préparation de Guanidines possédant en outre une fonction "Ammonium quaternaire") by A. Lespagnol, E. Cuingnet and M. Debaert, Faculté de Pharmacie, Université, Lille, France.

The prepared components comply with the general formula given below:



We have put to use the action of a primary amine on S-methyl-isothiourea for grafting the guanidic grouping. This method necessitated the preliminary preparation of both primary and tertiary diamines, which were obtained by the reduction of tertiary nitrile amines. The quaternization constitutes the final phase.

LIVER EXTRACTS

Differences Between the Biological Activities of Liver Extracts Prepared by Various Processes, (Différences entre les activités biologiques d'extraits de foie préparés par différents procédés) by E. Mascitelli-Coriandoli, Laboratorio Ricerche Farmavigor S. p. A., Milano.

The various processes of extraction produce liver extracts which, aside from their vitamin B_{12} content can be made to have noticeably different effects, observable by the study of special metabolic conditions experimentally induced in laboratory animals.

By examining the alcohol-soluble parts of total aqueous extract of liver, of papain lysate and pepsin lysate of liver and their phenolic refined products, several of these differences can be noted.

In the first series of experiments conducted on rats nourished for four weeks on a diet containing 0.4% P in the form of NaH_2PO_4 we were able to ascertain that a modest increase of hepatic concentrations of cytochrome C (greatly reduced by this diet) is detectable only with alcohol-soluble parts of liver lysates, with the vitamin B_{12} content equivalent to the other types extracted. By phenolic refining this property is greatly reduced.

In a second series of experiments, performed on mice nourished on a basic diet of oxydized casein, the maximum effect on corporal growth, choline-oxidasic activities and liver transmethylasic, is confirmed by the alcohol soluble part of pepsin lysate.

Even in this case the alcohol-soluble parts of the aqueous extract and the papain lysate lose their effect through phenolic refining.

RECTAL TAMPONS

Testing of the Absorption of Medicaments Applied by Means of "Recto-Tampons," (Contrôle de l'absorption de médicaments appliqués au moyen de "Recto-Tampons") by P. Kramer, S. A. des Produits Paul Kramer, Lausanne, Suisse.

"Recto-Tampons" are a means of rectal application of medicaments in which the surface of absorption is reduced to the mucous membrane of the anal canal, exclusive of the actual rectal mucous membrane. A club-shaped tampon of absorbent cotton, mounted on a flexible stem of polyethylene, contains the medication in a hypertonic solution. It is equipped with a stop which prevents the tampon from sliding into the rectum. In this way the major part of the medication goes into the body by way of the vena cava, whereas that applied by means of suppositories passes mainly through the vena porta.

A first series of absorption tests were made by means of I^{131}, of which the arrival in the thyroid gland is measured by Geiger counter. The comparison with the absorption obtained by suppositories shows that this last is about 2 times that obtained by "Recto-Tampon" application. On the other hand, the maximum obtained with suppositories is reached at the end of about 2 hours, while it is necessary to wait at least 24 hours in order to observe the maximum when "Recto-Tampons" are used; although the latter are withdrawn 2 hours after application. This seems to indicate a "storing" of the medicament at the place of application and its slow discharge into the body. This phenomenon is particularly visible on graphs obtained from a hyperthyroid person. This has its importance when "Recto-Tampons" are used in the treatment of local ailments such as hemorrhoids, pruritus ani, etc.

A second testing series consists in measuring the amount of medication contained in the "Recto-Tampons" and in comparing this amount with that in identical tampons after use. The results of several of these measurements are given.

Hypertonicity is obtained by adding to the medicines incorporated in the tampons 0.10 Gm. of glucose. The tampon, which must be soaked in water before being used, retains about 1 ml. which gives a 10% solution. On the other hand, the absorption obtained with non-hypertonic tampons is practically nil.

NOSE DROPS

Physiological Testing of Nose Drops, (Contrôle physiologique des gouttes nasales), by Cl. Gallay, Laboratoire de Pharmacie Galénique, Université, Genève.

Up to now the pharmacist has scarcely taken notice of the preparation of nose drops, their analytical testing or even their influence on organisms, even though the use of them is considerable among the general public.

The present work is limited to the physiological testing of this type of medicine. For this we have chosen a warm blooded animal, which permits a better comparison with man. The guinea pig and the rabbit are particularly suitable. The tests tend to eliminate the excipients which paralyze the ciliary movement of the epithelium in the isolated trachea of the guinea pig. Thus we have established that hypotonic solutions both acidic (pH < 4.5) and oily are incompatible with the ciliary movement, these later being noxious by a natural toxicity and not by their viscosity.

The results of these experiments seem to indicate that for nose drops it would be preferable to use solutions which are isotonic, buffered at pH 6.8 (physiological pH), viscosified by methylcellulose (only the aqueous solutions have a tendency to carry infection into the natural cavities of the nose, thus giving rise to sinus inflammations!).

CURRENT LITERATURE

. . . also calling your attention to the following articles appearing in recent hospital and pharmaceutical journals

. . . . . .

ADMINISTRATION

—Cost of Drugs

Superstine, Edward and Weipert, Regina: Inpatient Pharmacy Charges, *Hosp. Management* 90:83 (July) 1960.

Vance, Joe: The Effect of Drug Costs on Hospital Costs, *South. Hosp.* 28:57 (July) 1960.

—Stock Control

McKinley, James D.: Floor Stock Control, *Am. Profess. Pharm.* 26:389 (June) 1960.

EDUCATION

Stauffer, Isabel: Advanced Training for Hospital Pharmacists, *Hosp. Pharm.* (Canada) 13:107 (May-June) 1960.

Lamertsen, Eleanor C.: The Pharmacist's Role in Nursing Education, *Hospitals* 34:57 (June) 1960.

PARENTERAL SOLUTIONS

Nelson, Kenneth R.: Application of Closed System Injection and Blood Sampling Units, *Hosp. Management* 89:92 (June) 1960.

PUBLIC RELATIONS

Anon.: Public Relations for the Hospital Pharmacist, *Hosp. Pharm. (Canada)* 13:62 (Mar.-Apr.) 1960.

RADIOISOTOPES

Curley, H. P.: Nuclear Sterilization, *South. Hosp.* 28:27 (June) 1960.

DRUG EVALUATIONS

by the Council on Drugs of the American Medical Association

► THE FOLLOWING MONOGRAPHS and supplemental statements on drugs have been authorized by the Council on Drugs of the American Medical Association for publication and inclusion in *New and Nonofficial Drugs*. They are based upon the evaluation of available scientific data and reports of investigations.

The issue of the *Journal of the American Medical Association* from which each monograph has been taken is noted under each monograph. Monographs in this issue of the JOURNAL include those published in the *A.M.A. Journal* for May 28, 1960.

Notice

New and Nonofficial Drugs 1960 is now available from your local bookstore and from the publishers, J. B. Lippincott Company, Philadelphia, Pa. This 1960 edition contains monographs of drugs evaluated by the Council on Drugs of the American Medical Association and published in the Journal of the A.M.A. to October 17, 1959. The indexes listed below contain those drugs evaluated and published between October 24, 1959 and May 28, 1960.

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REPORT TO THE COUNCIL

The Council has authorized publication of the following report.

H. D. KAUTZ, M.D., *Secretary*

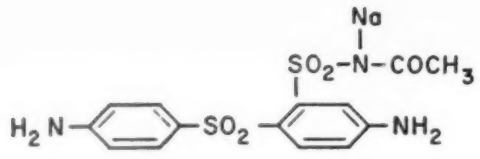
Current Status of the Therapy of Leprosy

JAMES A. DOULL, M.D., *Washington, D.C.*

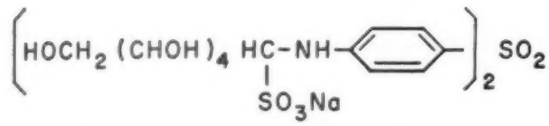
► IN THE SEARCH for a cure for leprosy, scientists are deprived of two of the most powerful tools of the experimental laboratory—a method of cultivation of Mycobacterium leprae and a susceptible animal. If the leprosy bacillus could be cultivated on an artificial medium, the bactericidal action of drugs and antibiotics might be determined rapidly, and, if a true prototype of human leprosy could be produced in animals, the effectiveness of drugs might be studied in an even more convincing manner. In the absence of such a direct approach, the most logical leads are to be found in the action of drugs on those pathogenic mycobacteria that can be cultivated and against mycobacterial diseases that are transmissible to laboratory animals. Advantage has been taken, in particular, of information that has been gained in the "screening" of drugs against Mycobacterium tuberculosis and in the treatment of patients with tuberculosis and experimental tuberculosis. Analogy with tuberculosis has failed in many instances, most notably in the case of isoniazid (Armazide, Cotinazin, Dinacrin, Ditubin, Inh, Isoniazid, Niconyl, Nicozide, Nydrazid, Rimifon, Tisin, Tyvid), but it has led to the successful use of the sulfones, streptomycin, and certain diphenyl thioureas in leprosy in humans.

In the preparation of this paper, liberal use has been made of recent reviews, especially those of Bushby,[1] Buu-Hoi,[2] Lechat,[3] and Sharp and Payne.[4] The description of the chemical structure of the sulfones, their pharmacology, toxicity, inhibitory capacity, and effectiveness in experimental infections (see figure) are slightly modified from those of Chang, Wolcott, and Doull.[5]

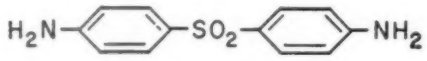
From the Medical Department of the Leonard Wood Memorial (American Leprosy Foundation).



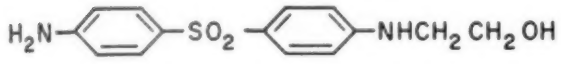
SODIUM ACETOSULFONE (PROMACETIN)



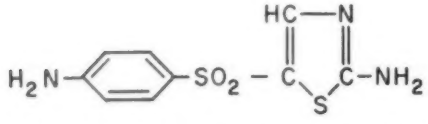
GLUCOSULFONE (PROMIN) SODIUM



PARENT SULFONE



HYDROXYETHYL SULFONE



THIAZOLSULFONE (PROMIZOLE)

Chemical structures of various sulfone compounds.

Incidence of Leprosy

Leprosy is an uncommon disease in the continental United States, the known prevalence being fewer than 1,000 cases. It occurs indigenously at a low level in southeastern Texas, still lower in Louisiana, and rarely in southern California and Florida (Key West). Occasional cases are detected among immigrants from areas in which the disease is endemic and among missionaries, educators, veterans of the military services, and others who have lived temporarily in such areas. When the known cases in Hawaii, Puerto Rico, and American Samoa are added, the total count is still well below 2,000. Despite its low prevalence in the United States, leprosy excites the interest of American physicians because of its unique history, the complexity of its clinical syndrome, its great public health importance in many countries—the world total being estimated at 10 million—and the challenge which its unsolved problems offer to science.

Classification of Types of Leprosy

Although leprosy is a generalized infection, the more manifest lesions are those of the skin, the mucous membranes of the upper respiratory tract, and certain peripheral nerves. In 1848, Danielssen and Boeck,[6] the Norwegian pioneers, described two principal clinical forms, tuberous (nodular) and anesthetic. In 1894, Hansen and Looft[7] changed the latter name to maculoanesthetic. This exclusively clinical classification was dominant for many years, although the nodular type became known as cutaneous and later as lepromatous, and the maculoanesthetic type was often called neural. The division was a useful one, but, since damage to peripheral nerve trunks and its sequelae occurred sooner or later in the nodular (cutaneous) type, many cases were thrown into a third category (no longer valid) called "mixed leprosy." This terminology was unsatisfactory, but further knowledge was required before classification could be put on a sounder basis.

Developments came on three fronts. With increasing study of the clinical varieties in different parts of the world, it became evident that there were cases which had been classed as nodular or cutaneous that were, in fact, different from the usual lepromatous ones. These had clearly delimited, erythematous nodulations or plaques which tended to progress peripherally and to resolve centrally, with central anesthesia. It also became evident that maculoanesthetic cases having anesthetic macules, with elevated, slowly progressing margins, were related to them. Histologically, it was demonstrated that these lesions all showed a characteristic tuberculoid structure and not the well-known lepromatous picture. The introduction of the lepromin (Mitsuda-Hayashi) test, which consists of the intradermal injection of a suspension of heat-killed, bacillus-rich, lepromatous tissue, was another important event. This test almost always caused reactions in patients showing these varieties of anesthetic plaques and macules; in the classical and more severe lepromatous type, the reaction was negative, suggesting that the form of disease which developed in the infected person depended primarily on tissue reactivity, signifying the presence or absence of resistance. These observations—clinical, histological, and immunological—provided a basis for a more satisfactory classification.

As the culmination of acts of several preceding international conferences since 1930, the Sixth International Congress of Leprology held at Madrid in 1953 adopted the present "official" classification scheme with definitions of two major (polar) types, lepromatous and tuberculoid, and of two supplementary classes or groups, borderline (cases between the two types) and indeterminate (cases with simple macular lesions).

Lepromatous cases are the most serious and most infectious, Myco. leprae being readily demonstrable in smears from the skin lesions and the nasal mucosa of patients. The lepromin reaction is negative. More or less extensive thickening of the skin is always present in well-established cases, and definite nodulation occurs with varying frequency. The borders of the lepromatous infiltrations are ill-defined. There may or may not be definite disturbance of sensation within the area of the lesion. The histological structure observed in the skin is granulomatous in nature, typically with Virchow cells (bacillus-laden histiocytes) which tend to become foamy as they age. As the disease progresses, the larger nerve trunks are invaded, especially the ulnars and peroneals. Anesthesia, atrophy of skin and muscle, absorption of the small bones of the hands and feet, ulceration, and natural amputation then follow; the ultimate destruction is equal to the worst that may be seen in the tuberculoid type of leprosy.

In the tuberculoid type, the characteristic macules have well-defined, more or less elevated margins, showing clearing at the center. The surface is often papillated. Anesthesia is invariably present within these lesions. The lepromin reaction is usually positive. Myco. leprae is rarely demonstrable in smears from the quiescent lesions but may be present in considerable numbers in the larger tuberculoid ones during reactive phases. The histological structure is also granulomatous, but theres are no Virchow cells. The predominant cells are epithelioid, which form noncaseating foci, and giant cells of the Langhans type are frequent. The reactional lesions may sometimes invade the epidermis. The earliest signs ordinarily are macules, but sometimes the distal effects of invasion of nerve trunks are more conspicuous, such as contractures of the fingers and toes, wasting of the interossei, and anesthesia. At a later stage, the neural sequelae are the same as those described for the lepromatous type.

Probably because of greater interest in recent years, borderline cases, previously classified as lepromatous, are being reported with increasing frequency. Plaques may show

histological features of both polar types, but the tuberculoid picture, often atypical, predominates. Mainly, it is the mixed clinical picture which determines a diagnosis of this class. Smears are positive for bacilli, and the lepromin reaction is usually negative. These cases usually arise from tuberculoid ones as a result of repeated reactions, and they may become frankly lepromatous.

In the indeterminate class, the lesions are simple, flat macules which show some disturbance of sensation; smears may reveal small numbers of Myco. leprae. The lepromin reaction may be positive or negative. The histological findings are those of simple, chronic inflammation. These cases are capable of progression toward either the lepromatous or the tuberculoid type.

Clinical Evaluation Studies of Leonard Wood Memorial

The nature of leprosy makes it essential that therapeutic trials be adequately controlled; otherwise, drugs that have value but fall short of complete success may pass undetected and be discarded. Most emphasis has been placed on severe and advanced disease, but all gradations of lesions can be recognized from the small macules (which may disappear spontaneously) to the far-advanced nodulation of the lepromatous type. The course of leprosy is prolonged over many years, with a tendency towards arrest of the active process, but there may be many exacerbations and remissions. Clinical impressions of the value of any therapeutic procedure may, therefore, be erroneous. The density of acid-fast bacilli in the skin also is an uncertain guide; reduction occurs frequently in the course of time without specific treatment, and there is no reliable method of distinguishing between the living and multiplying bacilli and those that are dead.

In 1941, in the earliest trials of the sulfones for the treatment of leprosy, a small, controlled study was carried out by Faget and his associates[8] at the Public Health Service Hospital (National Leprosarium), Carville, La. In 1951, large scale studies of longer duration were commenced by the Leonard Wood Memorial in cooperation with leprosariums in Japan, the Philippines, and the Union of South Africa, with financial aid from the Public Health Service and several pharmaceutical manufacturers. Three series have been completed,[9] and the trials are still going on. Reference is made later to the results obtained with various drugs, but certain general features may be mentioned.

The recognized principles of controlled clinical trials have been adhered to as closely as possible. Identical experiments have been conducted in at least two widely separated institutions. Only patients with the lepromatous type of the disease have been included, and patients have been assigned to therapy groups at random by statisticians in the United States. The groups have always been closely comparable to one another in such background items as age, sex, prior therapy, and current clinical and bacteriological status. Nevertheless, after eight years of study, we still do not know whether the age or sex of the patient has any significant bearing on response to therapy, although we continue to take these factors into account. A more disconcerting fact is that we have been unable to demonstrate greater clinical progress with identical treatment in less advanced cases than in those in whom the disease was well established at the commencement of therapy. This is probably a reflection of the slowness of clinical improvement and of the difficulty in demonstrating improvement in lesions that are slight at the beginning. Bacteriological measurements have likewise been inadequate to indicate any significance which age, sex, and stage of disease may have on prognosis.

The double-blind type of experiment was applied in our fourth series, which was continued for two years. There were four groups in this experiment. Two groups were treated with sulfones which were readily detectable in the blood. (It was necessary to obtain agreement from the clinicians and consultants not to consult the laboratory records.) Patients who became worse were withdrawn from the study and were referred to a special consultant not connected with the tests, who was told in confidence the treatment that had been given in order that he might treat the patient rationally. An unexpected complication arose which identified one of the drugs and forced its discontinuance at the end of one and one-half years. This was the occurrence of blueness (still inadequately explained) in the lesions of patients treated with amodiaquine (Camoquin) hydrochloride. The agents used in the other three groups remained unidentified to the end of the two-year period.

Another troublesome feature in these trials was the failure of a substantial proportion of the patients (10 to 20%) to complete the prescribed courses of treatment. This occurs to a greater or lesser extent in all long-term studies. Fatalities were few. The chief reason for discontinuance of therapy was the overwhelming desire of some of the patients to leave the institution against medical advice. In every instance, the patient's reasons were examined critically to make certain that they were not related to improvement or worsening of the disease or to the side-effects of a drug. Ultimately, the best that we can do is to study the comparability of the groups when the study ends, with respect to background factors that are definite, measurable, and that were more or less equal at the outset.

Older Forms of Therapy

Chaulmoogra Oil.—The history of the treatment of leprosy with chaulmoogra (Hydnocarpus) oil is an illuminative example of the necessity for adequately controlled studies of therapies. For generations, this oil was the popular remedy, and its esters and other derivatives were in world-wide use for almost twenty-five years. Hundreds of favorable case reports appeared, with photographs taken before and after treatment and with imposing statistics of arrest of the disease. In 1930, a publication[10] from the National Leprosarium gave case reports for 65 recoveries, but these were credited to a variety of factors, in addition to specific treatment with chaulmoogra oil and its esters. Johansen and Erickson[11] reported that, in 1926, experienced leprologists at that hospital considered that definite improvement had followed the use of the oil or its esters in a sufficiently large percentage of cases to warrant continuation of the treatment. By 1938, improvement was still noted, "although a considerable number of the older advanced cases show retrogression."[11] In 1942, the impression persisted that the chaulmoogra oil products were of some benefit. By 1946, after chaulmoogra oil was used for five years along with the sulfones, the popularity of chaulmoogra preparations had declined, but they were still being used in certain types of cases. In 1947, their use was entirely abandoned at the National Leprosarium. At present, chaulmoogra oil is used at only a few centers, usually as a supplement to a sulfone. A treatment that had attained universal popularity among leprologists and patients alike has been relegated to the shelves of the historical library; its value remains uncertain because controlled studies were not made.

Metals.—Several antimony, arsenic, bismuth, mercurial, and gold compounds have been tried in leprosy, usually with detrimental results. Small doses of potassium iodide have also been used ineffectively by a number of leprologists. Merbromin (Mercurochrome) was subjected to an extensive trial at the National Leprosarium during the period from 1924 to 1925.[10] It was reported to be of value in checking rapid retrogression and in treatment of lepromatous ulcers. Antimony is still used in treatment of "reactions."

Dyes.—Various aniline and other dyes have been used therapeutically by intravenous injection (methylene blue,

trypan blue, and fluorescein). The end-results were disappointing. Certain of these dyes have an affinity for lepromatous lesions, and, in cases of the borderline class of lesions, methylene blue has been used to differentiate such lesions from those of tuberculoid structure.

Sulfones

Although p,p′-sulfonyldianiline (DDS) was synthesized in 1908 by Fromm and Wittmann during their research on chemical dyes, it was not until 1937, after the phenomenal effectiveness of sulfonamides had been demonstrated, that this compound was tried against infections in laboratory animals. It proved to be far superior to sulfanilamide in streptococcic infections in mice but was much more toxic. In 1938, according to reports published more than 10 years later, it was used in man in doses of 1 to 2 Gm. daily for the treatment of acute streptococcic infections; however, it caused severe hemolytic anemia, and use of this agent was abandoned.

In 1939, Rist[12] of the Pasteur Institute found that DDS had a much stronger bacteriostatic (in vitro) effect than a sulfanilamide against both human and avian types of the tubercle bacillus, and, in the same year, Rist, Bloch, and Hamon[13] reported favorable results with experimental infection of the avian type in the rabbit. Probably because of the toxicity observed in animals, these reports did not lead immediately to the trial of DDS as a therapeutic agent in either tuberculosis or leprosy.

In 1937, Tilletson and colleagues, starting with DDS, prepared a soluble and less toxic compound, glucosulfone (Promin) sodium. During the next two years, the effect of glucosulfone was studied in several infections, but the results were not spectacular. It was toxic when given orally, even in small doses, irritating when injected subcutaneously, but well tolerated when given intravenously.

The discovery of glucosulfone led to the use of sulfones in leprosy. The intervening and significant event was the publication on Oct. 30, 1940, by Feldman, Hinshaw, and Moses[14] at the Mayo Foundation, of favorable results with the drug in experimental tuberculosis in the guinea pig. This report came to the attention of Dr. G. H. Faget of the National Leprosarium who obtained a supply of the drug. In March of 1941, the first patients were treated in a study which eventually revolutionized the treatment of leprosy.[8]

In the sulfone compounds, the sulfonyl radical, $R\text{-}SO_2\text{-}R$, is combined with two carbon atoms, whereas in the sulfonamides, this radical, $R\text{-}SO_2NH_2$, is combined with one carbon atom and an amino group. The principal sulfones which have been used therapeutically may be classified as follows: (1) parent sulfone, *p,p′*-sulfonyldianiline (DDS); (2) disubstituted derivatives having a substituent in each amino group such as glucosulfone sodium (*p,p′*-diaminodiphenylsulfone-N,N′-di-[dextrose sodium sulfonate]), and other examples: sulfoxone (Diasone) sodium, solapsone (Sulphetrone), Hydnosulphone; (3) monosubstituted compounds having one free amino group such as hydroxyethyl sulfone (4-amino-4′-hydroxyethylaminodiphenyl sulfone), and other examples: succinylsulfone, Exosulfonyl (succinylamido-4-amino-4′-diphenyl sulfone), Succisulphone, or 1500F, and phenylglycine sulfone or sulfone Cilag; (4) nuclearsubstituted derivatives with two free amino groups such as sodium acetosulfone (Promacetin or Internal Antiseptic no. 307 [sodium 4,4′-diamino-diphenylsulfone-2-*N*-acetylsulfonamide]), and propiosulfone (sodium 4,4′-diaminodiphenyl sulfone-2-sulfono-propionamide; and (5) asymmetric sulfone with two free amino groups such as thiazolsulfone (Promizole) (2-amino-5-sulfanilylthiazole). The chemical structures for examples of these compounds are given in the figure.

Pharmacology.—After usual therapeutic doses, the sulfones may be found in all body tissues and fluids. The liver and kidneys contain relatively high concentrations. The approximate blood levels reached with therapeutic doses are: DDS and hydroxyethyl sulfone, 0.5 mg. per 100 cc.; sulfoxone sodium, succinylsulfone, and sodium acetosulfone, 1 to 1.5 mg.; and glucosulfone sodium and solapsone, 4 to 5 mg. These levels increase, roughly, with molecular weights.

Individual variations in absorption and excretion occur after oral administration among patients taking the same dosage. In general, DDS is considered to be completely absorbed, because 90% of the oral intake is found in the urine, and only a trace is detectable in the feces. Sulfoxone is about 50% absorbed; 48% has been found in the urine and 44% in the feces. Solapsone is poorly absorbed; 10% is found in the urine and up to 80% in the feces. Acetosulfone is likewise poorly absorbed; 25% is excreted in the urine, and a large proportion is passed in the feces. Thiazolsulfone is well absorbed and rapidly eliminated. As high as 800 mg. per 100 cc. has been found in the urine of patients taking 6 to 7 Gm. daily by mouth. The urine may become pink to cherry red in color. About 50% of monosubstituted compounds is excreted in the urine.

After parenteral administration, from 95 to 100% of glucosulfone is excreted in the urine. Blood levels drop rapidly, especially in the first two hours after administration, but, after a dosage of 2 Gm. or more, appreciable levels are present after eight hours.

Disubstituted compounds are usually retained in measurable quantities in the patient's blood for about 14 days after cessation of treatment and, sometimes, even for four weeks or longer. DDS is even more cumulative, especially after parenteral administration. The high concentration of sulfones in the bile is of interest because biliary excretion and reabsorption tend to prolong retention and may be responsible for sulfones occasionally being found in the blood or urine long after cessation of treatment. Regular rest periods during therapy are, therefore, advisable. Because of cumulation, sulfones administered in moderate doses once or twice a week have been found to give blood levels more or less equal to those attained by administration of smaller daily doses.

There has been discussion of the hypothesis that the action of disubstituted sulfones is attributable chiefly to liberation of DDS in the body. The toxicity of glucosulfone, when given orally, is thought to be caused by breakdown to DDS in the gastrointestinal tract, and high concentrations of free DDS have been found in the blood and urine of patients treated with other disubstituted compounds given by the oral route. When given parenterally, glucosulfone and solapsone present a different picture. Only small amounts of free DDS are found in the blood and urine. Monosubstituted (hydroxyethyl sulfone) and nuclear-substituted derivatives (acetosulfone) do not break down to DDS; they act as entire molecules.

Toxicity for Animals.—Given orally, DDS is 5 to 7 times as toxic for mice as is glucosulfone, 8 to 12 times as toxic as sulfoxone, and more than 30 times as toxic as solapsone and acetosulfone. Excitement is a prominent sign resulting from treatment with DDS. Mice maintained on such therapy often run continuously around in their cages, and, if released, will run off the table. Larger doses cause various degrees of paralysis, including difficulty in respiration. Cyanosis is common in domestic animals. In sheep, and less severely in dogs and goats, excitement, nervous nodding, twitching of the lips, and pyrexia are seen. These may be followed by convulsions and paraplegia. No involvement of the nervous system has been observed in cattle even after large doses. Hemolytic anemia has been reported in guinea pigs given glucosulfone and in rabbits after administration of solapsone. Direct destruction of mature erythrocytes is considered to be the cause; a more remote suggestion is that sulfones inhibit intestinal bacterial flora, thus interfering with synthesis of the vitamin B complex and causing a deficiency anemia. Studies on chronic toxicity caused by various sulfones in rats, guinea pigs, and cats indicate that solapsone and hydroxyethyl sulfone are the least toxic.

Inhibitory Capacity Against Mycobacteria.—Because of inability to cultivate Myco. leprae in vitro, opinions on bacteriostatic capacity are based on effect on other species of mycobacteria; most work has been done on Myco. tuberculosis. DDS was shown to be active against the avian type of tubercle bacillus as early as 1939. The sulfone with the highest bacteriostatic power against the human type of tubercle bacillus is DDS, which is about twice as active as hydroxyethyl sulfone and 10 to 25 times as active as glucosulfone. Para-aminobenzoic acid is antagonistic and is known to inhibit, in whole or in part, the action of glucosulfone against Myco. tuberculosis and the action of DDS against Diplococcus pneumoniae.

Effectiveness in Experimental Tuberculosis.—In addition to DDS and glucosulfone, hydroxyethyl sulfone has been found to delay death in guinea pigs infected with Myco. tuberculosis. Sulfoxone, solapsone, and phenylglycine sulfone are only slightly active in this respect, and acetosulfone is inactive. Evidence of synergistic effect has been obtained with combinations of streptomycin and various sulfones.

Effectiveness in Other Mycobacterial Infections.—The ulcerative skin disease of man caused by Myco. ulcerans is transmissible to rats and mice. Both DDS and streptomycin are markedly effective in repressing the experimental disease in mice. The disease of rats and mice caused by Myco. leprae murium resembles human leprosy somewhat, but the peripheral nerves are not involved. The bacillus has not been cultivated in vitro. A number of sulfones and certain other drugs have been shown to exert repressive action in the experimental disease but none has prevented death. In the mycobacterial enteritis of cattle and sheep known as Johne's disease, the sulfones are ineffective.

Clinical Use in Leprosy.—The trial of glucosulfone sodium at the National Leprosarium followed by only a few months a disappointing experience with sulfanilamide.[8] This drug cleared up secondary infections in certain cases, but it had no observable effect on leprous lesions after about three months. Toxic complications were thought to be more frequent and severe than those found in other infectious diseases after administration of sulfanilamide. Glucosulfone, likewise, was toxic when given orally to 10 patients, in doses of 500 mg. to 1 Gm. daily. Severe hemolysis occurred in some patients. Intravenous administration, however, was well tolerated—as had been the experience in other diseases. Moderate degrees of anemia continued to be frequent but were treated successfully with administration of inorganic iron. After 12 months of treatment with glucosulfone, the disease in 15 of the 22 patients had improved; in 6, it was stationary, and in 1, worse. Five patients had tested negative bacteriologically. Ulceration of the nasal septum was seen to heal, and there was improvement in laryngitis and in ease of respiration. In several patients attending the dental clinic, the lesions of the lips and of the soft and hard palate had healed.

Since it was recognized that spontaneous improvement may have played a part, the small controlled experiment, previously mentioned,[8] was carried out. Acetosulfone was given to 20 patients in oral doses of 300 mg. to 1 Gm. daily. The same number of patients, matched as to type and stage of disease, were given a placebo. After eight months, the condition of the acetosulfone-treated group was superior to the other, especially in regard to such complications as rhinitis, laryngitis, and lepromatous ulceration of the skin.

The search for sulfone compounds which could be given orally eventually yielded a considerable number. The first to be used extensively was sulfoxone sodium; this was first used by Muir[15] in Trinidad. Solapsone was produced a little later and also came into extensive use. Acetosulfone, thiazolsulfone, and several other compounds gave favorable results in early trials, but cost of production limited their use.

In 1947, Cochrane and associates[16] in India, on learning that mastitis of cattle was being treated with injections of DDS, the parent sulfone of all aforementioned derivatives, obtained a 25% suspension of DDS in peanut oil. This was given by subcutaneous injection to a small group of patients in a dosage of 5 cc. (1.25 Gm. of DDS) twice weekly. Severe anemia occurred in several patients and psychosis in a few, but there was no evidence of hepatitis. Shortly afterward, Lowe and Smith[17] administered DDS by the oral route in much smaller doses; there was little evidence of toxicity, and the treatment appeared to be effective. In recent years, DDS has largely replaced other sulfone compounds in the treatment of leprosy, chiefly because of its low cost. Many leprologists, especially those working in outpatient clinics in Africa, prefer to administer therapy by the parenteral route. There is no convincing evidence that the mode of administration of DDS influences its effectiveness or the frequency of erythema nodosum or other reactions of lepromatous leprosy.

Effectiveness of Sulfones.—It is only in the lepromatous variety that adequately controlled studies have been made, although the great majority of reports indicate good results in the cutaneous lesions of the tuberculoid type. In the lepromatous type, DDS has been shown to be equal to sulfoxone in studies lasting 48 weeks conducted by the Leonard Wood Memorial, and this conclusion can probably be extended to solapsone and other disubstituted compounds.

The greatest improvement observed in patients during sulfone therapy occurs in ulcerative lepromatous lesions of the skin and mucosa. Nasal obstruction, hoarseness, and other signs of involvement of the upper air passages are usually greatly improved within three to six months. Tracheotomy, which was formerly a common operation in large leprosariums, has become rare. Lepromatous ulceration of the skin heals fairly promptly, and, consequently, there has been a marked reduction in the use of bandages. Improvement in diffuse infiltration of the skin and disappearance of plaques and nodules take place much more slowly. Clinical improvement is not accompanied by characteristic histological changes. The histological picture becomes predominantly atrophic, resembling that which occurs in spontaneous remission, without treatment of any sort. The explanation may be that the sulfones eliminate bacilli from the blood vessels and blood stream, thereby preventing formation of new lesions and permitting natural recovery to take place. Cystic lesions of the bones of the hands and feet, presumably due to invasion by Myco. leprae, have improved with sulfone therapy.

Invasion of peripheral nerves probably occurs in all cases of leprosy; there is one school of leprology which teaches that the spread of the bacilli, on entrance through the skin, takes place along the fine fibers of the cutaneous nerves. In the tuberculoid type, the neural elements in the dermis are completely destroyed. The explanation is not clear because usually no bacilli, or rare ones, can be demonstrated. In the lepromatous type, however, there are many bacilli, and the destruction of nerve fibers may be explained by pressure from growth of lepromatous tissue. In both types, but particularly in the tuberculoid type, the enlargement of the ulnar, peroneal, and posterior occipital nerve trunks may be conspicuous. Repeated and extremely painful attacks of neuritis are common—especially of the ulnar. In this instance, splinting the arm and keeping it warm are always advisable. Nerve stripping has been advocated to relieve pain, but this is not of permanent value. Local injections of cortisone (Cortisone, Cortogen, Cortone) acetate and procaine hydrochloride, with or without hyaluronidase (Alidase, Diffusin, Hyazyme, Wydase), may be of value in lessening nerve destruction, if given when acute neuritis first appears.

By the time that many patients seek treatment, destruction of nerves has taken place. Contractures, atrophy of skin and muscles, extensive anesthesia (often of the glove and stocking distribution), perforating ulcer of the foot, and some absorption of the small bones of the hands and feet may already be present. These changes are irreversible, although transplantation of tendons and other surgical procedures, together with physiotherapy, can do much to restore function. The question as to whether sulfone therapy can prevent or limit nerve damage and its sequelae is of vital importance but is as yet unanswered.

Bacteriological negativity, as judged from microscopic examination of simple smears from the skin is slowly attained. After one year of therapy, about 90% of patients still have

positive smears, and, after five years of treatment, 40 or 50% may still have positive smear tests. Bacteriological improvement, however, is demonstrable in a high proportion after one year. Smears from the nasal septum improve but do not become negative as rapidly as was formerly thought. Septal ulcers become clean but often do not entirely heal and may continue to discharge bacilli in diminished numbers. In the first series of the studies of the Leonard Wood Memorial, in groups of sulfone-treated patients, bacteriological improvement was greater for nasal septum sites than for skin sites after 16 weeks and after 32 weeks of therapy, but this finding has not been consistent in our subsequent work.

Bacteriological improvement, even if short of negativity, may be of great public health significance. Rapid increases in prevalence of leprosy are rare; in fact, the disease usually appears to have difficulty in maintaining itself, and it has disappeared from many areas where it once was prevalent. The biological balance between man and the leprosy bacillus is a nearly even one—with a slight advantage for man. A substantial reduction in the output of bacilli, therefore, rather than total negativity of the patient, may be all that is required to initiate or accelerate decline of the disease.

The recommended dosages of the sulfones in common use are given in the table.

Toxicity and Side-Effects.—The sulfones have a high safety record. At Carville, La., more than 1,100 patients have taken one or another compound for prolonged periods without a single instance of fatality or serious illness attributable to the drug. This does not mean that sulfones and particularly DDS can be used indiscriminately, without medical supervision. In outpatient treatment of large numbers of patients in Nigeria and the Belgian Congo, a few fatalities have been attributed to administration of DDS. Jaundice has usually been present, and, while the fatalities may have been due to the drug, other causes of hepatitis have not been excluded. One fatal case of granulocytopenia has recently been reported after treatment of a patient for dermatitis herpetiformis with DDS.

The most commonly reported toxic effect is hemolytic anemia. In some cases, there has been confusion with anemias caused by malnutrition, intestinal parasites, and by uncomplicated leprosy. Secondary anemias caused by sulfones may

Drug	Route	Mg./Kg. of Body Weight: Initial	Mg./Kg. of Body Weight: Maximum*	Frequency[1]
DDS	Oral	0.5	3.0	Daily
DDS	Parenteral	1.0	8.0	Twice weekly
Sulfoxone sodium	Oral	3.0	20.0	Daily
Glucosulfone sodium	Intravenous	20.0	100.0	Daily
Solapsone	Oral	20.0	120.0	Daily
Solapsone	Intramuscular	5.0	30.0	Twice weekly

*Attained after an induction period of 6 to 8 weeks.

[1]In many institutions, daily doses are omitted on Sundays. For all preparations, rest periods of two weeks should alternate with therapy periods of three months.

be corrected by administration of ferrous salts alone or supplemented by liver extracts. Sometimes it is advisable to lower the dosage of sulfones for a few weeks, but it is rarely necessary to discontinue treatment.

Dermatitis, in a variety of forms, may occur. When this happens, treatment should be discontinued. Sometimes another sulfone is well tolerated after the rash disappears.

The urinary tract is remarkably tolerant to the sulfones. Patients who have albuminuria, however, may not be able to take full dosage and should be kept under close observation. Amyloid nephrosis has long been recognized as a leading cause of death at the National Leprosarium, but, for some unknown reason, it does not seem to be as common in foreign leprosariums. Advanced amyloidosis of the kidneys is a part of generalized amyloidosis and is a contraindication to sulfone therapy.

Relapses.—Relapses may occur in lepromatous leprosy after long and intensive sulfone treatment. It is probable that these relapses are lessened in frequency by continuation of treatment, but this has not been demonstrated. Permanent cure can never be assured, and it is recommended that patients whose disease is apparently arrested should continue on a low dosage of a sulfone for life.

Other Drugs

Sodium aminosalicylate (Pamisyl Sodium, Para-Pas Sodium, Parasal Sodium, Pasara Sodium, Pasem Sodium, Pasmed Sodium, Sodium *p*-Aminosalicylate, Sodium Para-Aminosalicylate) was tested against leprosy at the Westfort Institution, Pretoria, South Africa, during one of the clinical trials by the Leonard Wood Memorial. It was considered to have some activity and should be subjected to more extensive study.

Thioureas (Thiocarbamides).—After favorable reports by others, the Leonard Wood Memorial tested the value in lepromatous leprosy of a disubstituted thiourea, thiocarbanilide (4-butoxy-4′-dimethylaminodiphenyl thiourea). The trial was a controlled one, conducted over a two-year period in exactly the same pattern at each of two Philippine institutions. The drug was given in a daily dosage of 60 mg. per kilogram of body weight. There were three other therapy groups in the experiment, given, respectively, amodiaquine hydrochloride, 200 mg. daily; DDS, 4 mg. per kilogram of body weight; and DDS, 2.5 mg. per kilogram of body weight. After 72 weeks, the amodiaquine was withdrawn because it was clearly inferior to the other drugs. The thiourea appeared to be slightly inferior to DDS, but the only difference which was significant statistically was lesser improvement in the smears from the nasal septum. After 96 weeks, the clinical and bacteriological results at each institution both pointed to lesser value of the thiourea, and, when the data for both institutions were combined, this finding was definitely indicated. Nevertheless, the drug caused no toxicity and showed up well in this rigid test. Therefore, its use should be considered whenever sulfones are ineffective or not well tolerated. Buu-Hoi[2] has reported good results with another thiourea, 4,4′-diethoxycarbanilide (Dialid).

The thiosemicarbazones may be regarded as monosubsituted thioureas. One of these, amithiozone (Benthiozon, Conteben, Tibione), which has had rather a wide trial in treatment of tuberculosis, has been used in the treatment of leprosy by a number of workers. Early results were promising, but this was generally not true of the second and third years of treatment. In those instances in which clinical improvement continued to occur over a period of three years, attainment of bacteriological negativity was rare. Also, there were instances of serious toxic effects, including granulocytopenia, allergic dermatitis, and recurrent drug fever.

Mercaptan Compounds.—Certain mercaptan compounds have shown antituberculosis activity in mice, which has led to clinical trials in leprosy. The mercaptans or thioalcohols are mostly colorless volatile liquids with the odor of garlic, the elimination of which is still a problem. The activity is supposed to be due to liberation of ethyl mercaptan. In the treatment of leprosy, two preparations have been used: (1) sodium ethyl thiosulfate (ET) given as pills in a dosage of 1.2 Gm. daily and (2) diethyl dithiolisophthalate (ETIP, Etisul) given by inunction in a dosage of 5 Gm. three times a week. Preliminary reports have been favorable, and larger and more adequately controlled trials are contemplated.

Nicotinic Acid Derivatives.—Nicotinamide, in a maximum dosage for adults of 500 mg. daily, was given as a supplement to DDS in clinical trials carried out in an identical pattern at each of three leprosariums, two in the Philippines and one in the Union of South Africa. A reference group was treated with DDS. The nicotinamide group showed no advantage at the end of 48 weeks.

Isoniazid was tried by many leprologists after favorable reports, in 1952, of its value in tuberculosis. The reports are not all in agreement, but the consensus is that this drug is less effective than DDS. In a large-scale study (second series) of the Leonard Wood Memorial, isoniazid was used as a supplement to sulfoxone, but no additive effect was observed by the end of 48 weeks. It was also used in a small number of patients in combination with pyrazinamide,

but the results were no better than those observed in a reference group treated with DDS.

Isonicotinylhydrazone of 2-formyl-phenoxyacetic acid (Compound 377), which has a markedly repressive action in experimental tuberculosis in mice, was used in patients with lepromatous leprosy in a controlled study at the Westfort Institution, Union of South Africa, in a maximum dosage of 900 mg. per day. At the end of 72 weeks, patients treated with DDS showed somewhat greater improvement than those given Compound 377, as judged by both clinical and bacteriological standards.

Antibiotics

Streptomycin and Dihydrostreptomycin.—Streptomycin was first used in the treatment of leprosy in 1946, at the National Leprosarium.[11] The dosage was 2 Gm. daily given in eight divided doses, for four months. Improvement was noted especially in lesions of the mucous membranes of the upper respiratory tract, but toxic effects were severe and frequent. In the first series of the Clinical Evaluation Studies of the Leonard Wood Memorial, already mentioned, dihydrostreptomycin sulfate was given in a dosage of 1 Gm. three times a week to three groups treated, respectively, with dihydrostreptomycin alone, dihydrostreptomycin in combination with sulfoxone, and dihydrostreptomycin in combination with sodium aminosalicylate. A fourth group received sulfoxone alone; a fifth, DDS; and a sixth, the control group, received a placebo (in Japan and the Philippines) and sodium aminosalicylate (in South Africa). Clinical improvement occurred in about the same proportion of all groups at each center, except the one which was given the placebo at the Japanese and Philippine institutions. Bacteriological improvement occurred in all groups, including the controls, at all centers. It was concluded that sulfoxone, DDS, and dihydrostreptomycin were of definite and of equal value so far as judgment could be made after 48 weeks of therapy. The results were disappointing in that combined treatment with sulfoxone and dihydrostreptomycin, or with dihydrostreptomycin and sodium aminosalicylate, offered no additive advantage over sulfoxone, DDS, or dihydrostreptomycin given alone.

In the second series of the Memorial's studies dihydrostreptomycin was used in combination with isoniazid. Dihydrostreptomycin was given twice weekly in a dosage of 1 Gm., and isoniazid was given in a daily dosage of 10 mg. per kilogram of body weight. At the end of 48 weeks, this combination showed no advantage over sulfoxone used alone.

Penicillin.—Penicillin has been tried in leprosy at a number of centers, beginning in 1944, in doses which have varied from 25,000 units daily to 100,000 units. Massive doses have not been used. Treatment has been continued for varying periods, with a beneficial effect on the healing of nonleprous ulcers but with no effect on Myco. leprae or on the course of the disease.

Cycloserine (Seromycin).—Cycloserine has been used in several studies. In small, matched groups of lepromatous patients at two Philippine leprosariums, treated respectively with cycloserine and DDS for 48 weeks, the antibiotic showed some therapeutic action, but there was no evidence of superiority over the sulfones. Cycloserine was well tolerated by these patients.

Other antibiotics have received limited trials, and a positive statement regarding them cannot be made. Chlortetracycline (Aureomycin) hydrochloride showed good results in a small series at Carville, La., and chloramphenicol (Chloromycetin) gave negative results in a few cases in Cuba.

Nonspecific Vaccine Therapy

The opinion that natural reactivity to lepromin indicates some degree of resistance to leprosy has led to attempts to induce reactivity in lepromatous patients by artificial means. Acquirement of reactivity, associated with clinical and bacteriological improvement, has been reported to follow vaccination with a vaccine prepared from killed Myco. marinum, which was originally isolated from a leprous nodule. This series was uncontrolled, and the results have not been confirmed by others. Tuberculosis (BGG) vaccine has been used by a number of leprologists. In the third series of the studies of the Leonard Wood Memorial, repeated vaccinations with this vaccine did not induce reactivity in a significant proportion of the patients and had no effect on the course of lepromatous leprosy.

Treatment of Complications

Lesions of Eye.—In lepromatous leprosy, the bacilli lodge in the anterior segment of the eye, but the path of invasion is unknown. Nodules may appear in the conjunctiva and episclera. A type of superficial punctate keratitis marked by discrete interstitial opacities, without pain or disturbance of vision, is considered to be pathognomonic of leprosy. Ulceration of the cornea, pannus formation, and a sclerotic keratitis follow. The iris and ciliary body are usually affected, and chronic plastic iridocyclitis is the principal cause of blindness. Acute iridocyclitis is often associated with an attack of erythema nodosum.

The opinion is widely held by leprologists that sulfone therapy will prevent ocular leprosy or limit its progress. In the cooperative studies of the Leonard Wood Memorial, keratoconjunctivitis has cleared up with sulfone therapy, but new instances have also occurred. Further study of this important aspect of therapy is necessary. Cortisone is effective in the acute exacerbations of iridocyclitis and iritis. At the National Leprosarium, local applications have been useful. The consulting ophthalmologist, Dr. James H. Allen of New Orleans, uses cortisone acetate in a strength of 0.5%. Remission is only temporary, but the treatment appears to be equally effective in recurrences of the acute process. Whether lepromatous keratitis and iridocyclitis can be controlled indefinitely remains to be proved, but, in the meantime, pain is relieved, and possession of useful sight is prolonged.

In both the lepromatous and tuberculoid types, eye lesions may be secondary to nerve involvement. Anesthesia of the conjunctiva and cornea follows involvement of the ophthalmic division of the fifth cranial nerve. Unnoticed injury and painless corneal ulceration may ensue. Lagophthalmos follows damage to the temporal and zygomatic branches of the seventh nerve, and exposure keratitis may develop. Considering the frequency with which one or both of these nerves are involved, especially in the tuberculoid type, the number of patients who lose their sight in this manner is suprisingly small. Nevertheless, the advantages of tarsorrhaphy should always be considered.

Reactions During Therapy.—Repeated attacks of erythema nodosum are extremely common in lepromatous leprosy. Attention was first drawn to it in 1912. Raised, tender nodules may cover the face, trunk, and extremities and be accompanied by malaise, arthralgia, neuritis, and fever. Occasionally, orchitis occurs. The occurrence of erythema nodosum in leprosy is not related to any form of therapy. It has been frequent and at times severe in those treated with dihydrostreptomycin or a thiourea as well as in the sulfone-treated patients. In mild cases no special treatment is usually necessary, and chemotherapy may be continued. When fever is high or other constitutional symptoms severe, specific treatment should be discontinued and bed rest instituted. Scores of remedies have been advocated, of which antipyretics, antihistamines, and potassium antimony tartrate are the most popular.[3] Whether these drugs are beneficial is doubtful. In acute and severe cases, cortisone or another corticosteroid may be used in the minimal dosage required to control the reaction and may be continued for about a week after the lesions begin to subside. In these patients, relief of the pain of acute neuritis is often dramatic. There is no evidence that leprosy is worsened by short courses of treatment with these hormones. In chronic, recurring erythema nodosum, however, much more experience is needed. Recurrences are not prevented, and whether they are lessened or worsened in severity is not known. At the National Leprosarium,[18] parenteral administration of cortisone or corticotropin (ACTH, Acthar, Corticotropin, Cortophin) has been continued as long

as 10 months, in an attempt to control these reactions. In some patients, reactions persisted in spite of very high doses, but no serious complications had been observed to the time of report (1956). Controlled studies are necessary to evaluate the results of a long-term, low-dosage schedule as a supplement to sulfone treatment.

Progressive lepra reaction is much less frequent than erythema nodosum but much more severe. It is characterized by great extension of the cutaneous lesions, together with neuritis, high and long-continued fever, and cachexia. Since these progressive reactions threaten life, there may be no alternative to treatment with cortisone or corticotropin preparations. However, both physician and patient must recognize the probability that therapy may have to be continued for several months and must accept whatever untoward effects may ensue.

In the tuberculoid type of leprosy, the reactions are usually of shorter duration than in the lepromatous type and are thought by some leprologists to have a beneficial effect on the disease. They may, however, be alarmingly severe. The cutaneous lesions become reddened, and new ones appear. Myco. leprae is often readily demonstrable in smears from these lesions. As in the lepromatous type, neuritis, most frequently of the ulnar, is the most distressing feature. At times, it seems to be precipitated or worsened by sulfone therapy. Cortisone will control the pain temporarily, but further studies are required to determine whether it can lessen nerve damage and its sequelae.

Conclusions

The drugs of choice in the treatment of leprosy, taking both efficacy and cost into account, are those of the sulfone class. In suitable dosage, the parent sulfone, *p,p'*-sulfonyldianiline (DDS), gives the same results as any of the disubstituted compounds such as glucosulfone, sulfoxone, or solapsone. There are patients, however, who tolerate one of the latter better than DDS. There are also patients who do not respond satisfactorily to sulfone therapy. For these, dihydrostreptomycin or a diphenyl thiourea may be tried. In the lepromatous type, treatment should be continued indefinitely. In the tuberculoid type, there is a tendency toward spontaneous arrest, and, in many patients with only single macular lesions, specific therapy is not indicated. In active tuberculoid cases with multiple lesions, sulfones should be given, although evidence of their value is not conclusive.

The treatment of the reactions of leprosy constitutes the greatest difficulty, especially in the lepromatous type. It is true that in many such cases there is only erythema nodosum, with minor constitutional disturbance. This usually clears up without treatment. In other instances, the reaction is a progressive one, with severe constitutional symptoms and exacerbation of the leprotic lesions. The reaction may subside after weeks or months of illness. Sometimes it can be controlled with a corticosteroid compound. Certain cases baffle the skill of the physician, and death occurs from what is called "leprous cachexia," for lack of a better name.

The value of the sulfones in leprosy has been definitely established. Their effect, however, is bacteriostatic and not bactericidal. This conclusion follows from the slowness of clinical and bacteriological improvement and from the not infrequent occurrence of relapse after many months of treatment. Search for a more rapidly effective drug should be pressed with much greater vigor than is being done at present. The basic needs are a method of cultivation of the leprosy bacillus and an animal that is susceptible to the disease. Until at least one of these is found, the path of analogy is the most logical one to follow. Tuberculosis has been a valuable guide, but there are several other mycobacterial diseases which have been inadequately studied from the point of view of therapy. In addition, there are cultivable mycobacteria which have been very little used for screening. Every drug or antibiotic that shows significant action against any mycobacterium and is proved safe according to long-term toxicity studies should be tested in leprosy in humans.

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POSITIONS

in hospital pharmacy

PERSONNEL PLACEMENT SERVICE

The Personnel Placement Service is operated without charge for the benefit of hospitals and pharmacist members of the American Pharmaceutical Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS. The ultimate purpose is the improvement of pharmaceutical services in hospitals, by more adequately fulfilling hospital pharmacy personnel needs and by locating positions which provide challenging opportunities for pharmacists who have indicated an interest in a hospital career.

By participating in the service, the hospital indicates a desire to achieve a pharmaceutical service which meets the *Minimum Standard for Pharmacies in Hospitals.* A description of the position should be submitted to the Division of Hospital Pharmacy on the forms provided. The hospital will receive applications directly from the applicant. The hospital agrees to reply to each application received and to notify the Division of Hospital Pharmacy when the position is filled.

The pharmacist, by participating, agrees to submit a Personnel Placement Service Information Form to the Division of Hospital Pharmacy. The applicant will then be notified of openings listed with the Service as they become available and can negotiate directly with the hospital if he is interested. It is agreed that the Division of Hospital Pharmacy will be notified as soon as a position is accepted.

A listing of positions open and wanted will be made regularly in the AMERICAN JOURNAL OF HOSPITAL PHARMACY without charge. Neither the name of the hospital offering the position nor the name of the applicant will be listed, except by code. All inquiries should be directed as shown above, including the code number.
Address all inquiries to

Division of Hospital Pharmacy
2215 Constitution Avenue, N. W.
Washington, 7, D. C.

positions open

STAFF PHARMACIST—188 bed general hospital. Duties include filling patient drug orders and outpatient prescriptions, and assisting chief pharmacist. California registration desired. Forty to forty-eight hour week, vacation, sick leave and group insurance. PO-214

ASST. CHIEF PHARMACIST—380 bed general hospital located in Colorado. Duties include compounding, dispensing, maintaining stock of pharmaceuticals, and furnishing information concerning medications to physicians, interns, and nurses. Responsible for operation of pharmacy department in absence of chief pharmacist. Vacation, holidays and sick leave. PO-213

STAFF PHARMACIST—500 bed general hospital located in South Carolina. Duties include compounding and dispensing for individual patient orders and ward stock. Experience in hospital pharmacy preferred, but will consider a recent graduate. Forty-four hour week, vacation. PO-212

CHIEF PHARMACIST—190 bed community hospital located in Virginia. Applicant must have administrative ability as well as organizational ability. Must be interested in teaching. Close relationship with medical and nursing staff of the hospital. Forty hour week, vacation, sick leave and retirement plan. PO-211

STAFF PHARMACIST—335 bed general hospital located in Florida. Duties include filling requisitions from nursing stations and a large volume of outpatient prescriptions. Will assist chief pharmacist. Vacation, sick leave, free hospitalization and pension programs. PO-210

ASST. CHIEF PHARMACIST—220 bed general hospital. Will be in charge of pharmacy in chief pharmacist's absence. Qualifications: female, B.S., experience in pharmacy administration, licensed in Pennsylvania. Forty hour week, vacation, progressive personnel policy. PO-209

STAFF PHARMACIST—500 bed general hospital located in Iowa. Modern pharmacy. Pharmacist will work closely with medical staff and school of nursing. Male or female. Forty hour week, vacation, sick leave, and insurance. PO-205

ASST. CHIEF PHARMACIST—238 bed general hospital located in Michigan. Duties include dispensing, controlling pharmacy divisions on nursing units, and assuming responsibility of pharmacy in the absence of chief pharmacist. Forty hour week, vacation, holidays, and sick leave. PO-204

ASST. CHIEF PHARMACIST—204 bed hospital. Dutjes include dispensing, receiving, and labeling drugs, etc.; furnishing information to physicians and nurses; teaching student nurses; and being responsible as an assistant department head in administrative and other related duties. Forty hour week, vacation, insurance, and sick leave. Must be eligible for registration in Illinois. PO-203

CHIEF PHARMACIST—104 bed general hospital. Direct pharmacy with the help of full-time registered nurses and assist in the purchase of medical surgical supplies. Forty hour week, vacation, and sick leave. Located in a university town in Illinois. PO-202

STAFF PHARMACIST—280 bed general hospital. Intern and resident program, school of nursing and school of medical technology. Building program to include new pharmacy facilities. Must have B. S. in Pharmacy. Michigan registration required or be eligible for licensure. Recent graduate acceptable. Forty hour week, vacation, insurance, pension plan, holidays, and sick leave. PO-199

STAFF PHARMACIST—700 bed general hospital. Duties include filling prescriptions for inpatients and outpatients. B. S. required. Must be registered or eligible for licensure in Illinois. PO-196

CHIEF PHARMACIST—300 bed hospital located in Virginia. Pharmacist will have responsibility of organizing dept., purchasing initial stocks, planning policies and procedures, establishing formulary, and serving on Pharmacy and Therapeutics Committee. Forty hour week, vacation, and sick leave. PO-195

STAFF PHARMACIST—790 bed hospital. Duties include handling and filling of inpatient and outpatient departmental orders, outpatient prescriptions and bulk manufacturing. Must be registered or eligible for registration in Ohio. Male preferred. Forty hour week, vacation, holidays, and pension plan. PO-194

ASST. CHIEF PHARMACIST—225 bed general hospital in Hawaii. Assist chief pharmacist; charge of dept. in chief pharmacist's absence. Must be eligible for licensure in Hawaii. Forty hour week, vacation, holidays, annual sick leave, insurance, and retirement plans. PO-191

CHIEF PHARMACIST—2300 bed mental hospital. Pharmacist will have complete charge of pharmacy, drug orders, stocking, dispensing, compounding, necessary records, and other pharmacy duties. Must be licensed in Ohio. Forty hour week, vacation, holidays, insurance, retirement plan, and sick leave benefits. PO-189

STAFF PHARMACIST—325 bed general hospital located in Pennsylvania. Duties include filling requisitions from the various nursing stations for floor drugs and completing specific prescriptions to patients. Forty hour week, vacation, and group hospitalization. PO-186

STAFF PHARMACIST—400 bed general hospital located in Michigan. Excellent opportunity in an expanding pharmacy program. Liberal benefits. PO-185

CHIEF PHARMACIST—312 bed nonprofit community hospital. Male or female. Must be qualified and eligible for licensure in Virginia. Forty to forty-four hour week, vacation, and insurance plans. PO-181

CHIEF PHARMACIST—264 bed general hospital located in Texas. Plans and directs pharmacy policies, compounds and dispenses medicines, purchases supplies and materials, maintains records, and prepares periodical reports. Must be eligible for or have M. S. Degree. Forty hour week, vacation, retirement, sick leave, and insurance plans. PO-177

STAFF PHARMACIST—290 bed general medical and surgical city hospital. Duties include compounding, dispensing, manufacturing, and assisting in the purchasing of supplies. Prepares reports and maintains records. Furnishes information concerning medications to physicians and nurses. In absence of associate pharmacist will assist with special duties as assigned by chief pharmacist. Male or female between 23 - 45 years of age. Ohio registration required. Hospital pharmacy internship preferable. Forty hour week, vacation, sick leave, retirement plan, credit union, holidays, and insurance. PO-170

STAFF PHARMACIST—200 bed general hospital. Duties include compounding, dispensing, and manufacturing. Applicant must have B. S. in Pharmacy and be registered in Connecticut. Recent graduate acceptable. Forty-four hour week, vacation, pension plan, and hospitalization. PO-168

ASST. CHIEF PHARMACIST—102 bed general hospital located in Oregon. Pleasant surroundings in college city of 8,000 - 20,000 students. Male or female. Must be registered. Forty hour week, vacation, holidays, and sick days. PO-166

STAFF PHARMACIST—100 bed general hospital located in Texas. Assume personal responsibility for accurate filling of prescriptions and supplies, assist in inspecting drugs in nursing stations, replace stock taken from night emergency container, inspect and refill ophthalmic solution trays from operating room, emergency room, and central supply. Female preferred. Must be registered or eligible for registration in Texas. Forty hour week, vacation, holidays, and sick leave. PO-164

ASST. CHIEF PHARMACIST—280 bed general hospital. Duties include filling prescriptions and medication orders from various units, supervise pharmacy clerks, assume administrative responsibility when chief pharmacist is absent. Forty-four hour week, sick leave, and holidays. Must be registered in Illinois. PO-161

CHIEF PHARMACIST—103 bed general hospital. Purchasing, receiving and issuing of pharmacy supplies. Taking inventory once a year. Filling out various reports necessary to operation of dept., etc. Must be registered in Washington State. Forty hour week, vacation, holidays, sick leave, and insurance. PO-158

STAFF PHARMACISTS—Unique, new 400 bed general private hospital where pharmacists join the doctor-nurse team by working in a dispensing unit location on each 100 bed nursing unit or in the central pharmacy. The dispensing unit personnel have responsibility for providing drugs, oxygen, dressing trays, I.V. solutions and similar items. A total of sixteen staff pharmacists is required to staff the hospital. Applicants must be eligible for registration in California. Excellent opportunity; generous benefits. PO-148

STAFF OR ASST. CHIEF PHARMACIST—150 bed general hospital located in New Mexico. Generous benefits. PO-134.

STAFF PHARMACIST—500 bed general hospital located in Oklahoma. B. S. required. Forty hour week. PO-95

ASST. CHIEF PHARMACIST—315 bed general hospital. Registration in Iowa required. Experience desirable. Forty hour week, vacation. PO-92

ASST. CHIEF PHARMACIST—237 bed general hospital in West Virginia. Female desired. Forty-four hour week, vacation. PO-77

positions wanted

ASST. CHIEF OR CHIEF PHARMACIST—Male, married. Received at Ohio State University B.S. Degree in Biology in 1952 and B.S. Degree in Pharmacy in 1955. Five years' hospital pharmacy experience. Willing to locate in the Western, Northern or Eastern part of country. Registered in Ohio. PW-277

ASST. CHIEF OR CHIEF PHARMACIST—Female, single. B. S. obtained in 1956 at the University of Wyoming. Completion of work for M.S. Degree expected fall of 1960 at the University of Maryland. Served hospital pharmacy internship. Hospital pharmacy experience. Prefers to locate in the West. Registered in Wyoming. PW-276

STAFF OR ASST. CHIEF PHARMACIST—Female, married. B.S. obtained in 1954 at St. Louis College of Pharmacy. Six Years' hospital pharmacy experience. Prefers the Northwestern part of the country, but willing to locate anywhere. Registered in Missouri. PW-275

CHIEF PHARMACIST—Male, married. Obtained M.S. in Hospital Pharmacy in 1954 at the University of Southern California. Served hospital pharmacy internship. Eight years' hospital pharmacy experience. Prefers to locate in the Northeastern part of the country. Registered in New York, New Jersey and California. PW-274

ASST. CHIEF OR CHIEF PHARMACIST—Male, single. Obtained M.S. in 1959 at the Medical College of Virginia. Served hospital pharmacy internship. Military obligation completed. Will be available for employment during September. Prefers to locate in the East. Registered in New Jersey. PW-273

CHIEF PHARMACIST—Male, married. Received B.S. Degree in 1957 at Purdue University. Two years' hospital pharmacy experience. Tour of duty in U. S. Army will be completed in September. Prefers to locate in the Southeastern part of country. Registered in Indiana and Illinois. PW-272

STAFF PHARMACIST—Male, married. Obtained B. S. in 1952 at Duquesne University. Prefers to locate in the Pittsburgh area. Registered in Pennsylvania. PW-271

ASST. CHIEF OR CHIEF PHARMACIST—Male, single. M. S. obtained in 1958 at the University of Texas. Served hospital pharmacy internship. Hospital pharmacy experience. Prefers to locate in the Southwest. Registered in Kansas and Texas. PW-270

ASST. CHIEF OR CHIEF PHARMACIST—Male, married. B. S. obtained in 1955 at the University of Nebraska. Hospital pharmacy experience. Prefers to locate in the West or Midwest. Registered in Nebraska. PW-269

STAFF OR ASST. CHIEF PHARMACIST—Male, married. Ph.D. and B.S. obtained at the University of California. Two years' hospital pharmacy experience. Prefers to locate in California. Registered in California. PW-267

CHIEF PHARMACIST—Male, single. Obtained M. S. in 1954 at the University of Tennessee. Served hospital pharmacy internship. Six years' hospital pharmacy experience. Prefers to locate in the Southwest or in Florida. Registered in Connecticut and New York. PW-266

CHIEF PHARMACIST—Male, married. M. S. obtained in 1957 at the Nebraska University College of Pharmacy. Served hospital pharmacy internship. Six years' hospital pharmacy experience. Prefers to locate in the West or Midwest. Registered in Colorado, Missouri and Nebraska. PW-265

CHIEF PHARMACIST—Male, married. Obtained M. S. in Hospital Pharmacy at the State University of Iowa in June, 1959. Served hospital pharmacy internship. Three years' hospital pharmacy experience. Will locate anywhere. Registered in Illinois. PW-264

CHIEF PHARMACIST—Male, married. B. S. Served hospital pharmacy internship. Extensive hospital pharmacy experience. Prefers to locate in the Midwest. Registered in Ohio. PW-263

CHIEF PHARMACIST—Female, single. B. S. Thirteen years' hospital pharmacy experience. Prefers to locate in the Midwest or in the East. Registered in New York. PW-262

STAFF PHARMACIST—Male, single. Obtained B. S. in 1957. Hospital pharmacy experience. Prefers to locate in the East. Registered in Texas and Washington, D. C. PW-261

CHIEF PHARMACIST—Male, married. B. S. Fourteen years' hospital pharmacy experience. Prefers to locate in the East or Midwest. Registered in Pennsylvania and West Virginia. PW-260

STAFF PHARMACIST—Female, single. Obtained B. S. in 1958 at West Virginia University College of Pharmacy. Served hospital pharmacy internship at Duke University Medical Center. Two years' hospital pharmacy experience. Prefers to locate in the Northeast. Registered in West Virginia and North Carolina. PW-259

CHIEF PHARMACIST—Male, married. Received B. S. at Temple University School of Pharmacy in 1938. Completed hospital pharmacy internship at Jefferson Medical College Hospital in 1960. Prefers to locate in East. Registered in Pennsylvania. PW-258

STAFF PHARMACIST—Male, married. Obtained B. S. in 1952 at Purdue University. Hospital experience. Prefers to locate in Ohio or Indiana. Registered in Ohio and Indiana. PW-257

ASST. CHIEF PHARMACIST—Male, single. Obtained B. S. in 1956 at Purdue University. Hospital pharmacy experience. Prefers position with some administrative and/or teaching duties. Would like to locate in Northeast or Southwest section of country. Registered in Texas. PW-256

STAFF OR ASST. CHIEF PHARMACIST—Female, single. Obtained B. S. in 1952 at the University of Nebraska. Hospital pharmacy experience. Prefers to locate in the East, South or in Hawaii. Registered in Nebraska. PW-254

CHIEF PHARMACIST—Male, single. B. S. obtained in 1952 at the University of Illinois. Served hospital pharmacy internship. Two years' hospital pharmacy experience. Registered in Illinois. Prefers to locate in Arizona. PW-252

STAFF PHARMACIST—Male, single. Will obtain B. S. Degree at Oklahoma University. Prefers Oklahoma or surrounding states. Six months' hospital pharmacy experience. PW-250

CHIEF PHARMACIST—Male, single. Obtained Pharm. D. Degree in 1957 at the University of Southern California. Twelve years' hospital pharmacy experience. Registered in Minnesota and California. Prefers to locate in Minneapolis, Minnesota. PW-249

STAFF OR CHIEF PHARMACIST—Male, married. Obtained B. S. in 1959 at Medical College of South Carolina. Completed hospital pharmacy internship in June, 1960. Registered in South Carolina. Prefers to locate in Pennsylvania, Virginia or North Carolina. PW-248

ASST. CHIEF OR CHIEF PHARMACIST—Male, married. Obtained B. S. in 1954 at South Dakota State College. Two years' hospital pharmacy experience. Will locate anywhere. Registered in South Dakota. PW-247

STAFF PHARMACIST—Male, married. Received B. S. in June, 1960, at Philadelphia College of Pharmacy and Science. One year's hospital pharmacy experience. Prefers to locate in Philadelphia. PW-246

STAFF OR ASST. CHIEF PHARMACIST—Applicant has held government position as Director of Medical Services in Sierra Leone, West Africa, since 1958. Holds B. S. Degree in Pharmacy from Drake University and has taken special courses in Parenteral Products and Radioisotope Techniques at Philadelphia College of Pharmacy. Served hospital pharmacy internship at University of Arkansas Medical Center. Additional hospital pharmacy experience in England. Registered in Iowa. PW-245

CHIEF PHARMACIST—Male, married. Ph.C. Degree received at Ohio State College of Pharmacy. Twelve years' hospital pharmacy experience. Will locate anywhere. Registered in Ohio and Hawaii. PW-244

CHIEF PHARMACIST—Male, married. Obtained B. S. in 1953 at Ohio Northern University. Seven years' hospital pharmacy experience. Will locate anywhere. Registered in Ohio. PW-243

PHARMACIST—Male, single. Will obtain M. S. Degree in August, 1960, at State University of Iowa. Four years' hospital pharmacy experience. Prefers to locate in the New York City area. Registered in Iowa. PW-240

ASST. CHIEF OR CHIEF PHARMACIST—Male, married. Received M. S. Degree in 1960 at the State University of Iowa. Serving hospital pharmacy internship. Prefers to locate in the East. PW-239

STAFF OR ASST. CHIEF PHARMACIST—Male, married. Obtained B. S. in 1950. Presently working for M. S. Degree at the University of Maryland. Two years' hospital pharmacy experience. Prefers to locate in the East. Registered in Maryland. PW-238

DIRECTOR OF PHARMACY SERVICES—Male, single. Received B. S. in 1956 at the University of California. Served hospital pharmacy internship. Four years' hospital pharmacy experience. Registered in California. Prefers to locate in California. PW-237

ASST. CHIEF PHARMACIST—Male, single. Obtained B. S. at Xavier University in May, 1959. Will locate anywhere. Registered in Louisiana. PW-235

STAFF OR CHIEF PHARMACIST—Male, married. Obtained B. S. at St. Louis College of Pharmacy. Served hospital pharmacy internship. Three years' hospital pharmacy experience. Prefers to locate in Midwest. Registered in Missouri. PW-234

CHIEF PHARMACIST—Male, married. Obtained B. S. at Massachusetts College of Pharmacy in 1943. Nine years' hospital pharmacy experience. Prefers to locate in East. Registered in Connecticut and Massachusetts. PW-230

PHARMACIST—Male, married. B. S. received at Howard College of Pharmacy in 1956. Served hospital pharmacy internship. Two years' hospital pharmacy experience. Prefers to locate in Florida. Registered in Florida and Alabama. PW-227

PHARMACIST—Female, single. M. S. received at the University of Maryland in 1951. Served hospital pharmacy internship. Five years' hospital pharmacy experience. Prefers to locate in New Jersey. Registered in Pennsylvania and Missouri. PW-225

ASST. CHIEF OR CHIEF PHARMACIST—Male, married. B. S. received at Detroit Institute of Technology in 1950. Four years' hospital pharmacy experience. Prefers to locate in Michigan. Registered in Michigan. PW-224

CHIEF PHARMACIST—Male, married. B. S. received at the University of Wisconsin in 1957. Four years' hospital pharmacy experience. Prefers to locate in Wisconsin. Registered in Wisconsin. PW-222

ASST. CHIEF OR CHIEF PHARMACIST—Male, married. Received B. S. at Medical College of South Carolina in 1950. Four years' hospital pharmacy experience. Prefers Southeast section of U. S. Registered in North Carolina and South Carolina. PW-221

CHIEF PHARMACIST—Male, single. Received M. S. at University of Michigan in 1957. Six years' hospital pharmacy experience. Served hospital pharmacy internship. Will locate anywhere. Registered in Michigan and Ohio. PW-220

CHIEF PHARMACIST—Male, single. B. S. received in 1952 at Massachusetts College of Pharmacy. Seven years' hospital pharmacy experience. Will locate anywhere. Registered in Massachusetts. PW-218

STAFF OR CHIEF PHARMACIST—Male, single. B. S. received in 1952 at St. Louis College of Pharmacy. Two years' hospital pharmacy experience. Registered in Missouri. Prefers to locate on the West Coast, particularly California. PW-217

CHIEF PHARMACIST—Male, married. Received M. S. at the State University of Iowa. Served hospital pharmacy internship. Registered in Iowa. Prefers to locate in the Northern Midwest. PW-215

ASST. CHIEF OR CHIEF PHARMACIST—Male, married. B. S. received in 1954 at the Southwestern State College in Oklahoma. Served hospital pharmacy internship. Three years' hospital pharmacy experience. Registered in Oklahoma. Prefers to locate in the Southwest. PW-214

STAFF PHARMACIST—Female, single. B. S. Seven years' hospital pharmacy experience. Southwest section of country preferred. Registered in Alabama and Georgia. PW-199

ASST. CHIEF OR CHIEF PHARMACIST—Male, married. M. S. obtained in 1956 at Columbia University College of Pharmacy. Hospital experience. Prefers to locate in California. Registered in New York, Michigan, New Jersey and Florida. PW-184

ASST. CHIEF OR CHIEF PHARMACIST—Male. B. S. received in 1954. Desires to locate in Michigan, Ohio or Illinois. Registered in Michigan. PW-177

PHARMACIST—Female. Graduate of the University of Idaho, 1954. Registered in Illinois. Hospital experience. Prefers Chicago area. PW-166

ASST. CHIEF OR CHIEF PHARMACIST—Female. B. S. and M. S. Purdue University. Ten years' hospital pharmacy experience. Registered in Indiana and Kentucky. PW-164

PHARMACIST—Male. Registered in Louisiana and Missouri. Experienced. Prefers Midwest. PW-161

ASST. CHIEF PHARMACIST—Male, single. Registered in N. Y. and Vt. Served hospital pharmacy internship, now employed part-time staff pharmacist. Prefers Eastern part of country. Has M. S., four years' hospital pharmacy experience. PW-154

CHIEF PHARMACIST—Male, married. B. S. Ten years' hospital pharmacy experience. Registered in Mass., Ill., Mo., Ky., Tenn., and Va. PW-150

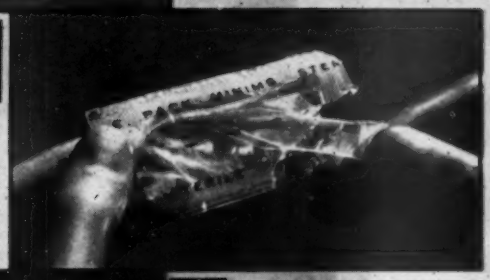
PHARMACIST—Male, single. B. S. received in June, 1959. Prefers to locate in East. PW-149

ASST. CHIEF OR CHIEF PHARMACIST—Single, male. Registered in D. C., Ill., Md., and Pa. Graduate University of Pittsburgh in 1953, experience in research. Prefers North and East. PW-148

CHIEF PHARMACIST—Male, married. Extensive experience as chief pharmacist and purchasing agent. Graduate of St. John's University College of Pharmacy. Prefers to locate in New York or New Jersey. Registered in New York and New Jersey. PW-144

ASST. DIRECTOR OR DIRECTOR OF PHARMACY SERVICES—Male, single. B. S. Retail and five years' hospital experience. Registered in Illinois. PW-119

CHIEF PHARMACIST—Female, single. Registered in Pennsylvania and Ohio. Twelve years' hospital pharmacy experience as a chief pharmacist. Desires to locate in Pennsylvania or Ohio. PW-111



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